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CARCINOMA OF THE LARYNX

JANEWAY MEMORIAL LECTURE*

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NEW YORK CITY

I APPRECIATE much more deeply than you realize, and for many reasons, the honor and privilege of addressing you here this evening.

In the first instance, this lecture is in commemoration of the work of my former Chief—the late Dr. Henry Harrington Janeway. I believe I may properly, and with some feeling of personal pride, claim the distinction of being, in addition to two faithful secretaries, his only assistant.

If this lecture were being given, as usually, within the intimacy of the American Radium Society membership, I should like to make it more informal and tell you something of the life and experiences with Harry Janeway during those earlier years of experimental work with radium. The setting this year, however, demands that I forego such informality and attempt to present to this international gathering a subject in which he had a very keen interest and to which he made substantial contribution.

With the rising hopes attendant upon the dawn of the irradiation era, the very handicap of total laryngectomy at once made laryngeal cancer a problem for study from the radiation standpoint.

As time has gone on, therapeutic radiologists have, as a group, come to make less and less distinction between true cancer of the larynx, cancer of the so-called extrinsic larynx, and cancer of the hypopharynx.

The second reason for selecting the subject of carcinoma of the larynx for this lecture is in an effort to make a sharp distinction between the clinical problems attendant upon its treatment and those pertaining to treatment of cancer of the hypopharynx.

In order to do this, reference must first be made to the anatomy of the throat.

In Figure 1, *1a* shows the anatomic landmarks of importance; *2a* shows by location of the x-marks those parts generally accepted as belonging to the larynx proper, usually referred to as intrinsic larynx. These are the vocal cords, the laryngeal surface of arytenoid cartilages, the ventricular bands or false cords and the adjacent ventricular folds, the ventricle or sinus of Morgagni and the subglottic zone above the cricoid level; *3a* shows in the same way the parts usually referred to as making up the extrinsic laryngeal area, namely, the external surface of the supporting framework of the larynx. By some, the entire epiglottis as well as the pyriform sinuses are included.

Anatomically, and as a clinical cancer problem, the epiglottis stands as a separate entity. The sinuses on either side, at the base of the epiglottis and slightly forward

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to it—the valleculae—belong to the base of the tongue. The pyriform sinuses, while mesial to the thyroid alae, are distinctly a part of the hypopharynx in general. The same is true of the posterior surface of the cricoid. As a matter of fact, growth in this in character from within the laryngeal box, outward. Stratified squamous epithelium covers the true cords, laryngeal side of epiglottis and anterior surface of the ventricles. Beyond this it shades outward into a stratified columnar ciliated epithelium

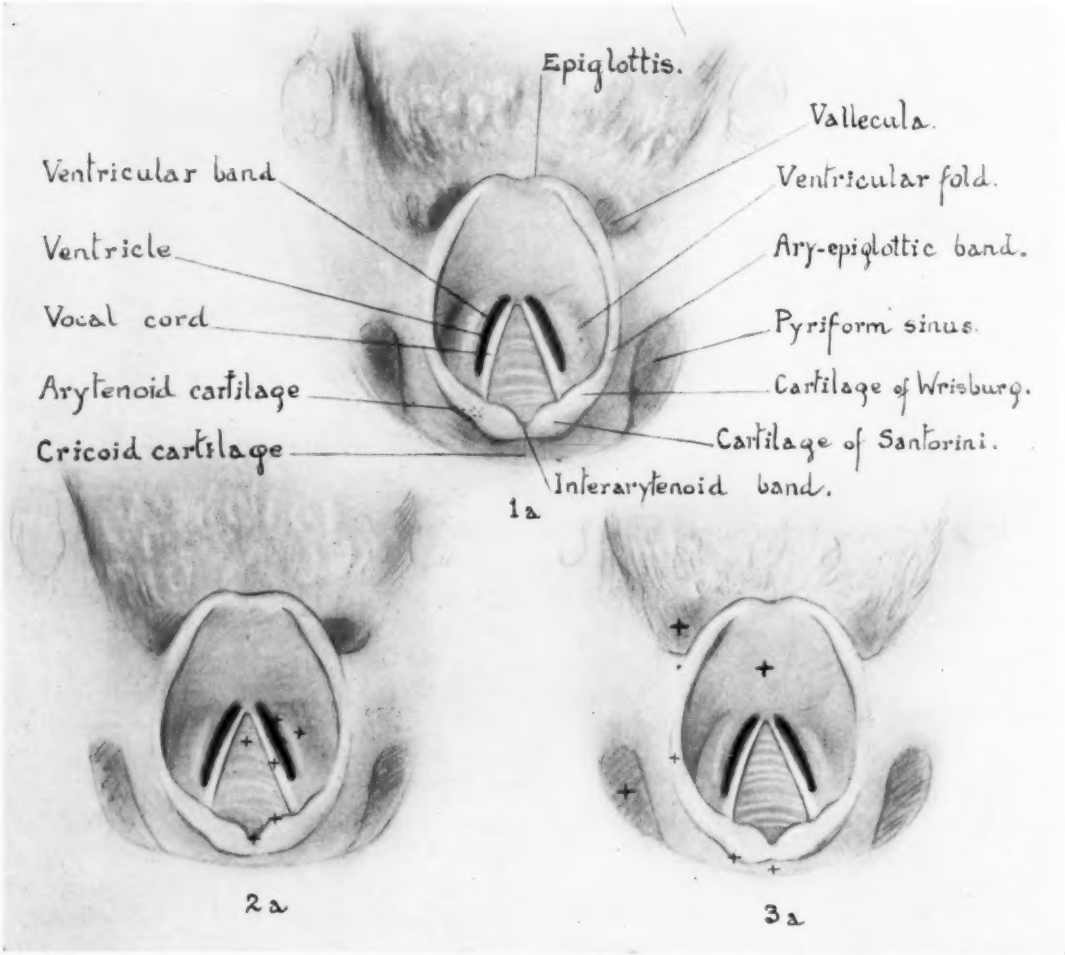


Fig. 1. *1a*, shows the anatomic landmarks of importance; *2a*, shows by location of x-marks those parts generally accepted as belonging to the larynx proper, usually referred to as intrinsic larynx; *3a*, shows the parts usually referred to as making up the extrinsic laryngeal area.

latter area more often than not manifests itself by symptoms referable to the esophageal inlet—by dysphagia. Negus[24] has shown that, with the esophagus attached over a considerable extent of the posterior cricoid surface, this, and the action of the cartilages of Santorini, serves to open the esophagus as the larynx closes.

The normal histology changes somewhat not unlike that of the nares. Lymphoid cells, singly and in islands, are to be found in the stroma. There is practically no muscularis mucosa. Tubular glands lined by serous and mucous cells are to be found in the submucosa. The hyaline cartilage tends to become calcified after the twentieth year but not the yellow elastic cartilage. This probably accounts for the seem-

ingly greater resistance of the former to tumor invasion. Clinical experience and relative frequency of growth types suggest that the relative radioresistance decreases from within the laryngeal box outward, rather in keeping with the changing normal histology. Certainly the surgical operability follows this trend from within outward over the gross anatomy, and from larynx proper to the so-called extrinsic laryngeal parts.

The frequency of cancer beginning primarily over these latter anatomic parts is much less than in the larynx proper. Many growths, loosely attributed to primary location within the border of the laryngeal ring, are found, on more careful examination, to be primary within the larynx proper and simply spilled over by direct extension to the outer zone.

Metastases are much more frequent and earlier in appearance from cancer usually referred to as extrinsic laryngeal. This may presumably be due in part to the difference in normal histology of the tissues of origin but chiefly to the more generous lymphatic drainage of the outer zone. The larynx proper has a very meager anastomosis of its lymphatic network with neighboring parts. The channels empty into two nodes on either side of the larynx, one beside the trachea and the other below the greater cornu of the hyoid bone.

For many reasons, therefore, it would avoid much confusion if the terms extrinsic and intrinsic were discarded, leaving two groupings of origin only; namely, cancer of the larynx (formerly intrinsic larynx, with its inlet "funnel") and cancer of the hypopharynx. I hold no controversy with those who may wish to classify the postcricoid area with the esophagus. The epiglottis represents an entity by itself.

Cancer of the larynx refers to those growths primary within the "funnel" of the larynx and the laryngeal box down to the cricoid level. Formerly the distinction has been vague and is becoming more so in the language of therapeutic radiology. Cancer of the larynx is being confused too much, clinically, with cancer of the hypopharynx. It is time we drew a heavy line of distinction, therapeutically, between the two.

Surgery of growths here classified as of hypopharyngeal origin has always given uniformly poor results and has been ungrudgingly turned to irradiation by all laryngologists—other than a few who will have none of it under any circumstances—with these we have neither time nor reason for debate. The relative radiosensitivity of the majority of malignant growths of the hypopharynx is well known.

The anatomic limits of cancer of the larynx, as here outlined, have represented the limits of serious surgical endeavor for nearly a century. The remarkable advance of laryngeal surgery since the beginning of the twentieth century has been accomplished entirely within this zone. It is a compact unit made up of a variety of tissues in intricate but nice adjustment.

We are prone to regard it simply as the voice box. In his monumental work on the comparative anatomy and physiology of the larynx, Negus takes the view that voice is largely peculiar to and highly specialized only in man. Through the entire range of mammals he attributes to it many and varied functions—chiefly, that of protecting valve to the lungs.

The problems in clinical medicine attendant upon cancer in this limited zone are many, located, as it is, at the gateway to two body systems. Interference with function of these systems is a serious handicap to therapy by whatever means. It is reasonably difficult of access and just beyond the range of one of the most valuable aids to diagnosis—direct palpation—except with an instrument. Normal drainage is in an unfavorable direction, and once an ulcerating lesion is present, the complicity of small and delicate structures tends toward the harboring of infection.

While cancer was recognized by the Ancients and considerable of aggressive treatment given external cancers from that time onward, it would seem that laryngeal

growths shared in the obscurity of most other internal tumors until a much later date. This seems peculiar when we consider the pronounced symptomatology as well as relative frequency.

Data on frequency vary considerably, depending upon the source. Ewing[9] has placed a range of 1–5 per cent of all tumors and adds that 16 per cent of all laryngeal tumors are cancer. Sir St. Clair Thomson[32] gives cancer of the larynx as 1.8 per cent of all cancers.

In their compilation of all Memorial Hospital, New York, statistics over a twelve-year period, Pack and Lefevre[26] have found laryngeal cancer in the male 5.3 per cent of all cancers, but only 0.48 per cent in the female. This places the ratio between the sexes at 10.4 to 1. They also found it to be 12.176 per cent of all cancers of the upper mucous membrane tract. These figures represent probably as accurate a cross-section as can be found, although any large clinic is bound to have a relative preponderance of certain case groups over others. Many of the older compilations listed as sarcoma a goodly number of cases which we now recognize as of epithelial origin, and likewise a substantial number rated as papillomata were probably papillary types of carcinoma.

It is difficult to determine just who first recognized laryngeal cancer as such. Certainly it was known in the eighteenth century but no treatment was attempted other than the various medical concoctions of the day, together with aggressive use of counterirritants externally.

In the *Medical Communications of London*, 1790, James Carmichael Smyth,[30] Physician Extraordinary to His Majesty, gave a most interesting report of a case which he saw in consultation, made a diagnosis of tumor of the larynx, and later obtained the gross specimen by limited autopsy. He finally termed it a "schirrhous"—the term then in use for non-painful cancer.

Early in the nineteenth century thought turned toward some form of surgical relief for laryngeal obstruction. Desault[23] of Paris first suggested it in 1812 although he never actually carried it out.

To Brauers[23] of Louvain goes the credit for the first division of the thyroid cartilage in the midline to gain direct access to the interior of the larynx for treatment of a tumor. It was a papilloma and he did not remove it, preferring to cauterize it. No tracheotomy tube was used and the operation preceded the use of anesthesia. The patient lived twenty years but ultimately died of cancer. This operation was done in 1833.

In 1844 Ehrmann[23] of Strassbourg removed a papilloma by division of both thyroid and cricoid cartilages. He did a preliminary tracheotomy two days before and removed the tube again the day following his main operation. The wound was closed by adhesive and healed in three weeks. The patient, however, died of typhoid seven months later.

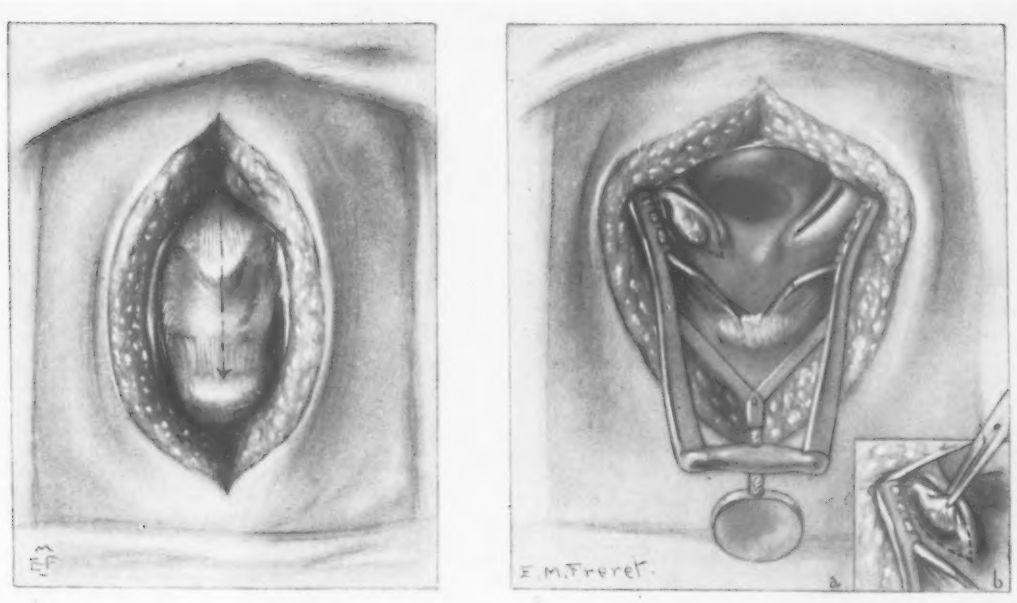
Soon considerable controversy arose over terminology for the various midline exposure operations. Without going into detail of all terms employed, it is probably most acceptable to use the term thyrotomy or median laryngotomy for simple division of the thyroid cartilage in the midline, and laryngofissure where both thyroid and cricoid are divided.

Figure 2 illustrates the thyrotomy exposure. If the cricoid is also divided, it is best referred to as laryngofissure.

Figure 3 shows a characteristic defect after limited surgery through the thyrotomy exposure.

For many years after Brauers' original operation, most of the operative approach was by laryngofissure. Cricoid division is not desirable unless a matter of necessity—it is apt to weaken the main support of the larynx.

The first operation on the larynx to be done in America was by Gurdon Buck,[2] surgeon to the old New York Hospital, in 1851. His detailed report is so fascinating that I trust I may be pardoned for reviewing it at some length.



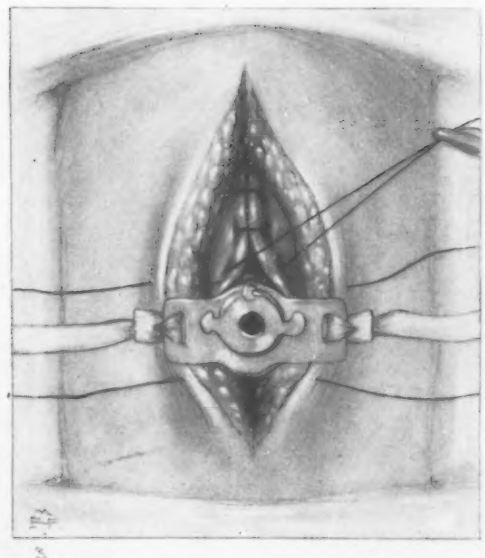


Fig. 2. Illustrates the thyrotomy exposure.

The patient, a widow, aged fifty-one, and living on Hoyt Street in Brooklyn, had been seen by Buck in consultation during the earlier part of her illness. She was then suffering from hoarseness and some dyspnea. Silver nitrate locally and external counterirritants were advised.

Some months later he was called to her home in consultation because of extreme dyspnea. After a very careful examination and extremely logical differential diagnostic discussion, which finally came down to either laryngeal tumor or aneurysm, the latter was finally excluded. Buck had recently read Ehrmann's monograph on "Histoire des polypes du larynx" published in 1850. Impressed by this, he advised operation. It was accepted by the patient and planned for Saturday, May 3, 1851, 12 o'clock noon, at the patient's home and in the presence of seven consultants.

The patient was seated in a low arm chair before a window, forward legs of the chair elevated on 3-inch blocks, and head tilted as far backward as her short fat neck would permit.

A 4-inch midline incision was made down to and through partially calcified thyroid and cricoid cartilages. Air rushed in and voice became extinct. The sides were retracted and bleeding controlled by pressure from a piece of sponge. The tumor looked like a condyloma. Parts were cut away but the oozing of blood and constant cough from blood trickling down the trachea exhausted the patient, although she "displayed remarkable courage." The wound was packed with sponge and a trachea tube put in.

The following day at the same hour the operation was resumed. Little headway was made; the surface was cauterized with acid nitrate of mercury, wound packed and tube reinserted. Buck then did some investigating on a cadaver and decided that by carrying his incision higher and into the base of epiglottis he might get the tumor out.

The next day at 1:30 P.M. and in the presence of eight consultants, he initiated his third attempt. However, the parts were so edematous that nothing much could be distinguished, and patient was unable to swallow. Wound was packed and tube reinserted. Two days later she could again swallow and improved steadily for a time. Tracheotomy tube was even corked temporarily.

No anesthetic was employed for any of these procedures.

tube in lower. A 5-inch incision was made and tube reinserted at level of the episternal notch. Dysphagia and earache soon became severe, secretions were very annoying. In March she coughed up an arytenoid cartilage.

On August 4, 1852, at 3 A.M. the patient removed the tube to clean it, could not reinsert it and quickly expired.

A limited autopsy permitted of removal of larynx, trachea and esophagus and an excellent color plate is published with Buck's report.

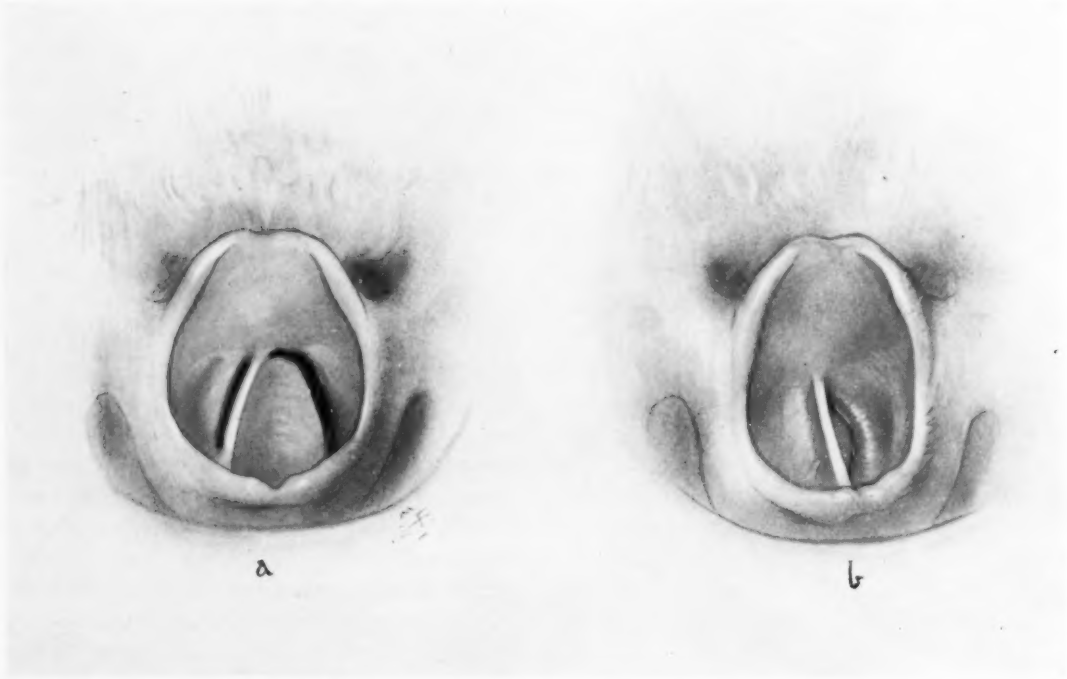


FIG. 3. Shows a characteristic defect after limited surgery through the thyrotomy exposure.

As dyspnea recurred, another operation was requested by the patient and done September 20, in the presence of eight consultants. It was Buck's hope to accomplish what he had failed to do on the third try. Scar tissue was cut away and incision carried to within 1½ inches of the chin and 1 inch below tracheotomy wound. Removal was impossible. He pared away enough tumor to permit introduction of a finger from below upward into the throat. Tube was reinserted, wound closed by three stitches, and steam inhalations ordered. "The Patient bore this operation with the same fortitude as the first." The wound healed by primary union.

After three months the dyspnea was recurring, bleeding and scar tissue contraction was very distressing and Buck decided to put the

Dr. H. Van Arsdale, microscopist to the New York Hospital Museum gave a detailed description and reported "the structure may therefore be regarded as non-malignant per se, and to belong to that class of morbid growths known as epithelial." Buck himself regarded it as a polyp. From the histology described and the published color plate, I am convinced that it was a papillary type squamous cell carcinoma. Irwin Moore[23] of London has expressed the same opinion.

After this experience, Buck's final recommendation to the American Medical Association was tracheotomy plus caustic applications of either acid nitrate of mercury or silver nitrate by mouth and thy-

rotomy when symptoms called for it.

It might be well if some of the critics of our earlier efforts with radium would familiarize themselves with the detail of this, and similar case reports dealing with the early surgery on behalf of the sufferers from laryngeal cancer.

Buck did a second operation for papilloma in 1862, this time successfully; no anesthetic was used.

H. B. Sands[28] of New York did a preliminary tracheotomy and laryngofissure and removed a carcinoma of the larynx in 1863. The larynx remained free of disease but the patient died twenty-two months later with a metastatic kidney. The case is of interest because it is the first in this country where a diagnosis of cancer was made before operation with the aid of a laryngeal mirror illuminated by direct sunlight. It is also the first recorded, done under ether inhalation since the introduction of this anesthetic by Morton in 1846.

The following year, 1864, Ulrich and Lewin[33] of Berlin did two thyrotomies for papilloma under chloroform anesthesia—the first recorded since Simpson introduced chloroform in 1847.

Sir Morell Mackenzie[21] of London did the first thyrotomy under local anesthesia in 1868 using anhydrous sulphuric ether as a spray directly on the tissues of the neck.

In England, one of the first, if not the first, tracheotomy for symptomatic relief of cancer was done in 1856 by Curling.[5]

A subsequent autopsy and histologic report by Andrew Clark, a popular and meticulously careful histologist of that period, is indeed quite modern in descriptive detail.

The tracheotomy tube had of course long been known and in use for various inflammatory conditions. We are indebted to Sabatier[27] for a good early history of its use in 1796. Harbicot used it in the early seventeenth century and prior to that Fabricius ab Aqua-pendente (1537–1619) had found it of value.

In the same way, the simple laryngeal mirror had been experimented with a good deal before Czermak[22] developed and popularized it in 1857. Babington[14] and many others had made efforts in that direction but met with little encouragement from their associates.

In 1854, Garcia,[12] a French singing-master in London, curious about the vocal cords and sound production, developed the mirror but presumably the scarcity of sunlight left it unpopular in that city. Czermak used artificial light and made it practical.

Gurdon Buck's first thyrotomy, here recorded in detail, was decided upon before the mirror was in use. His second case, 1862, was apparently diagnosed by mirror preoperatively, but not definitely so stated.

The direct laryngoscope[17] is of course of very much more recent date and for the refinement of its development we are chiefly indebted to Chevalier Jackson.

George Duncan Gibb[13] of London did the first removal (or partial removal) of laryngeal cancer by thyrotomy in England in 1864. Chloroform was used and the surgical approach was excellent. When it came to removal of the growth, however, the instrument employed was the finger nail of the left index finger. Gibb made a woodcut of his tumor and again Andrew Clark gave an interesting histologic description.

From that period onward cases were reported with increasing frequency. Arthur Durham[8] of Guy's Hospital, London, did a good many. Many were done on the Continent and in this country.

The results were not good and more and more criticism was expressed until, after an extensive review, Paul Bruns[1] of Berlin in 1878 published the conclusion "that the attempt at radical extirpation of cancer by means of thyrotomy has proved itself completely unsatisfactory and worthless."

Meanwhile, more radical efforts were being considered.

In 1868 Patrick H. Watson[11] of Edinburgh did the first total laryngectomy—the tumor proved to be a syphilitic granuloma and the patient died.

The idea, however, appealed to Czerny,

an assistant of Billroth. He did some experiments on dogs and demonstrated its practicability. In 1873 he assisted Billroth in doing the first total laryngectomy for cancer. Gussenbauer[15] devised an artificial phonation box for this case but the patient lived only a few months.

The first case in America was done by Frederick Lange[18] of New York in 1879. The patient, however, committed suicide within a week. In reviewing some of the earlier work, Delevan[7] has noted that suicide was not an infrequent sequel to these operations.

Radical efforts as well as the more limited types, however, were being carried on in many centers.

Delavan,[7] in his review, states that something of a crisis occurred on the Continent in the consideration of laryngeal cancer treatment during 1887–1888. The Crown Prince of Germany showed evidence of laryngeal disease. Many questions of state were involved in the decision as to treatment. If the decision was for operation, it would be done by von Bergmann. His material was reviewed and of 7 cases done, the average length of postoperative life was nineteen weeks—the longest, a year and a half. Operation was refused, the hope of Emperor Frederick carrying on for more than a year was thus realized, and the rights of his successor assured.

The notoriety of this case was said to have stimulated the study and practice of laryngectomy on the Continent.

At the same time it marked a dividing point between two schools of thought. The English preferred thyrotomy. Billroth[15] had done the first hemilaryngectomy in 1875 but this type of operation was nowhere especially popular. Gluck[7] of Berlin did some of the best early work in developing the total extirpation.

Later, J. Solis-Cohen[31] of Philadelphia, following Gluck's improved methods, did the first successful laryngectomy in America in 1892. The patient remained free of disease for many years and was finally lost track of in Ireland. Before going there, however, he spent many years in an almshouse. Solis-Cohen's was the most outstanding early work in this country.

That wonderful gentleman, and Dean of American laryngology, Dr. D. Bryson Delavan of New York—always a conservative, but strong supporter of all things progressive in laryngology—took an active interest in both types of operation.

In 1895, he took Solis-Cohen's case to London to demonstrate before the Section of Laryngology of the British Medical Association,[6] not only the Gluck type of operation with trachea brought forward and attached to the skin, but the excellent audible whisper the patient had developed by swallowing air and then utilizing it to produce pharyngeal and oral phonation.

Delavan made a plea for the pooling of these important operations and having them done only by a few of the most experienced and able operators, in the hope of obtaining, thereby, better results. His suggestion met with scant support. It was evident that everyone wished to try his hand at laryngeal operating.

The most outstanding English cancer surgeon of the closing nineteenth century, Sir Henry T. Butlin[3] was strongly in favor of thyrotomy and did more than any other of his time to improve it. His technical improvements were such that he had no postoperative deaths after 1899. His assistant and associate, Sir Felix Semon, did little to improve on Butlin's work.

It was, however, most ably carried forward by Sir St. Clair Thomson whose work still stands at the top of English laryngeal cancer surgery. In his monograph published in 1930, Thomson[32] cited 70 cases of laryngofissure in which he had, after excluding 3 operative deaths and cases dying of other diseases before three years, a three-year curability rate of 76 per cent. He was very conservative on total laryngectomy and, like practically all able operators of the present day, opposed to hemilaryngectomy.

While the results and experiences of nineteenth century laryngeal cancer surgery

were darker than the record of early radiation experiences, they at least formed a background for brilliant work in suitable cases after the turn of the century. As late as 1900 Delavan had been unable to find any reliable and encouraging statistics.

Reference has already been made to the contributions of Thomson in England.

It is impossible, here, to give adequate recognition to the work of the many able laryngeal operators in America. Chevalier Jackson[16] and his associates have shown remarkable results in the more conservative types of operation in suitably selected cases. They have been cautious in their position toward total laryngectomy and open minded in their attitude toward radiation therapy.

The work of MacKenty[20] stands out in the forefront for total laryngectomy. A gentleman of great skill, meticulous for detail, and with a broad preliminary general surgical training, he brought the principles of von Gluck and Solis-Cohen to a point of near perfection. At the time of publishing his monograph (1927) he had, in a group of 102 laryngectomies, in carefully selected material, three-year freedom from recurrence in 79.4 per cent.

In looking for an average statistical balance by good laryngeal operators of unquestioned surgical judgment, one cannot do better than refer to the figures of New[10,25] and his associates, or Fielding Lewis.[19] The former have reported 73 total laryngectomies of which 41 (56.1 per cent) have passed the five-year mark of freedom from disease. In a group of 83 total laryngectomies, Lewis has 53 (63 per cent) living, of whom 32 cases (38.5 per cent) have passed five years.

In spite of all these brilliant figures in carefully selected cases, we still have to face the facts. The encouraging statistical data represent the work of a few outstanding surgeons. The material from which such results are obtained must be carefully selected. No reliable statistical cross-section is available to show how many cases fall outside this list of selected material by the time a diagnosis of laryngeal cancer is made.

In the successful total laryngectomy we still have the loss of voice. In the successful thyrotomy or laryngofissure we still have the voice substantially impaired.

It was from this perspective that Dr. Janeway[34] and I, twenty years ago, took up the problem of relieving laryngeal cancer by irradiation. The problem was one of extending the saving of life to a larger group and of preserving function to a greater degree.

The earlier years were full of unhappy experiences. To begin with, there was no accumulated clinical experience with radium to serve as a background. On the roentgen-ray side, the same was practically true of 90 kv., 4 mm. Al filtered radiation. The physics of radiation had, as yet, little of the practical to offer and biophysics had scarcely been thought of.

We were in a maze of empiricism. There was plenty of advanced and hopeless cancer at our disposal—the type available to new and prospective remedies.

The first radium applications were made externally with cumbersome brass and lead-filtered tubes placed on 1-inch blocks to afford distance. Several of these blocks strapped together with adhesive were called a "pack." Later these packs were made of lighter material and increased to varying distances.

For internal surface applications a hook was attached to one end of the tube to fix it in the tissues and several inches of string tied on to safeguard it and permit of its withdrawal. Needless to say, these were of no value.

A change to 1 mm. platinum and 0.5 mm. silver tubes had the advantage of decreasing size and permitted of placing them tandem fashion in a long rubber tube. Under cocainization and with the aid of opiates, these could be introduced through the remaining lumen of larynx and kept in place for a little time. They were usually coughed up but we were able to show some gross tumor regression.

Histologic study of the tissues thus treated indicated that something peculiar was happening.

Various efforts were made to fashion intralaryngeal applicators which could be kept in place long enough to administer certain dosages visualized as of probable value. Neither then nor since have any such bits of apparatus been successful.

Late in 1916, Failla produced capillary glass seeds containing radon and soon we were using them extensively—perhaps too extensively. They were producing effects and results, by implantation in the more accessible tumors, far beyond anything we had previously observed. These we implanted in and about laryngeal tumors through a direct laryngoscope—occasionally with a curved trocar needle guided by indirect laryngoscopy.

It is needless to go into a description of the intense local inflammatory reactions, tissue sloughs and complications attendant upon such treatment. They are well known even if too often exaggerated and overemphasized. Review of the clinical material which survived years afterward cannot help but impress one with certain favorable features. The reactions, while severe, were localized. The resulting scars were unusually pliable. Considering the advanced character of the disease, the survival rate was unusually good.

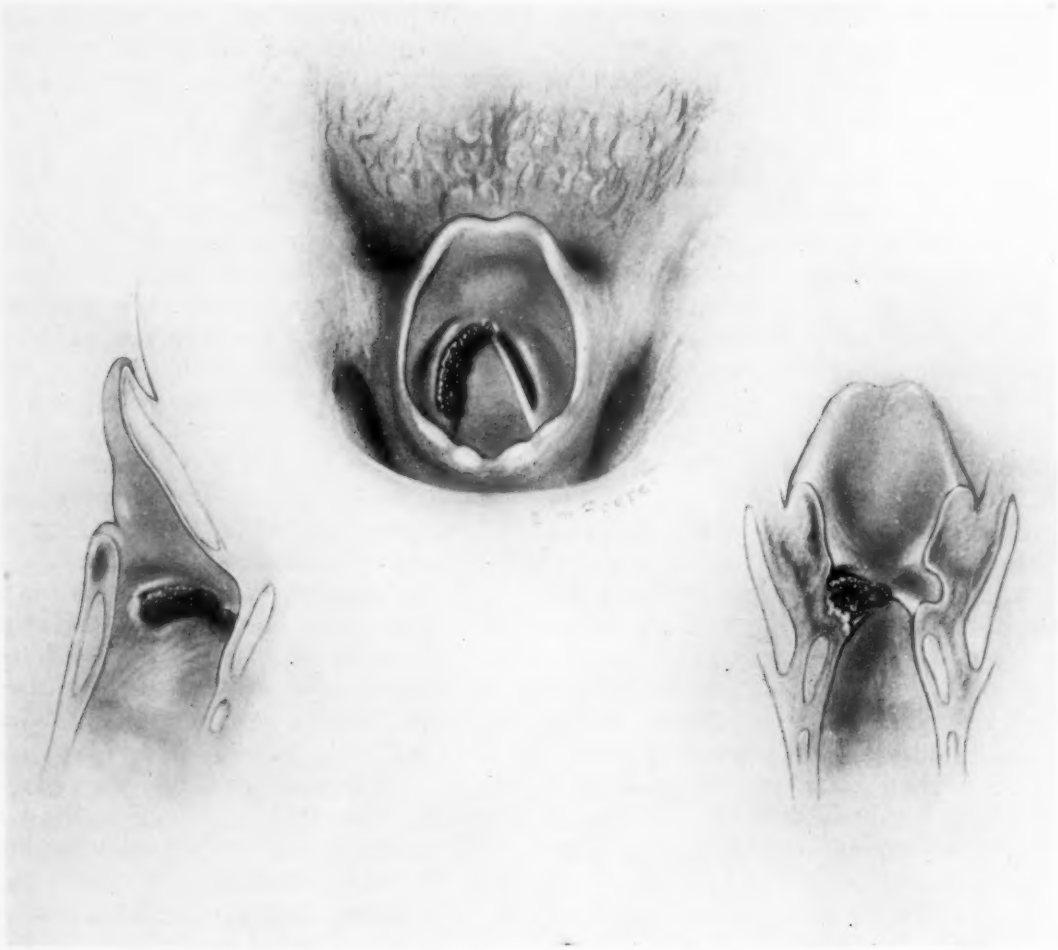


Fig. 4*a*. Case 1. This gives a visualization, in three planes, of the extent of the growth.

Viewed in retrospect, I have often felt

that the strength of radon, per individual seed, was too great and that the method would have gone much farther had it not been for this error.

The following case report will serve as an example.

Case 1. July 22, 1921. Male, aged fifty-two. Patient had suffered from progressive hoarseness for many months, becoming much more severe and accompanied by pain for one month; some dysphagia.

Examination showed a rather flat, ulcerating growth involving entire left cord and anterior commissure. It extended into ventricle and slightly below cord but not over posterior surface of the arytenoid. The mobility of arytenoid was markedly limited (Fig. 4*a*). Section showed a squamous cell carcinoma, infiltrating and predominantly Grade II (as later graded in a review) (Fig. 4*b*).

Treatment was by radon trays, 2 mm. brass plus 0.5 mm. silver filter and at 3 cm. distance, 2,000 mc-hr. to each side of larynx. This was followed immediately by implantation of unfiltered glass radon seeds through a direct laryngoscope—5 mc. total.

Growth regressed, but not completely, and three months later, another 5 mc. of unfiltered radon was implanted in the same manner. Improvement continued, after a sharp local reaction, but was still not complete.

Seven months later, the tray doses were repeated and two weeks thereafter a third dose of 5 mc. unfiltered radon was implanted by direct laryngoscopy.

The inflammatory reaction became marked but there was no gross necrosis. However, a low tracheotomy became necessary after three months. The inflammatory reaction gradually subsided and after a year the tube was kept corked part of the time. After another two years, the tube was removed and a persistent tube sinus was closed surgically in May, 1926.

The patient has been free from growth for fifteen years and from the tracheotomy tube for twelve years.

Comment. The case is cited to show some of the complications as well as tedium and pain of earlier radium treatment.

We were well aware of the desirability of greater filtration but were never impressed by the value of platinum-filtered

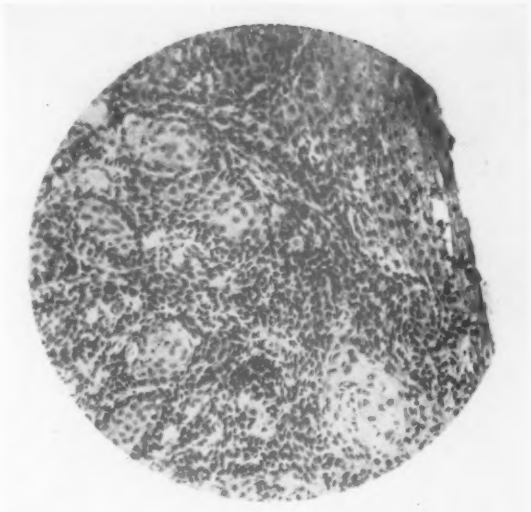


Fig. 4*b*. Case 1. Photomicrograph showing the histopathology of the tumor.

element needles in the larynx. We tried them in various ways but, like the various intralaryngeal tube arrangements, we could not depend on their staying in place.

The flexibility of the free implant had much in principle to commend it.

When the first high voltage roentgen therapy became available in this country, it was, of course, tried on cancer of the larynx but with no favorable result. It failed to produce any favorable impression in the laryngeal cancer field then for one of the same basic reasons, but in exaggerated manner, that a good deal of the present-day therapy falls short of being efficacious.

The so-called "massive dosage" of that period was nothing more than a magnified error of the too-heavy individual daily dose of today. The filter and distance was just as good as it is in many clinics now. The rate of delivery was better because the tubes were not as good, and consequently would not stand as much.

After a great deal of tedious experimental work, Failla was able to seal radium emanation in a capillary gold seed by the latter part of 1924. With this I carried on clinical experimental work in readily accessible tumors during the next few

months. The initial filtration was 0.2 mm. and later increased to 0.3 mm. gold.

The clinical reactions were less severe from an inflammatory standpoint and tissue necrosis much less frequent.

The filtration permitted of using a much greater gamma-ray dose. Again, the error was made of using seeds of too great individual strength. The average was about 2 mc. per seed. At a much later date, in my personal work, and in conjunction with more effective external therapy, the individual seed value was reduced to 1 mc., or less in many instances.

During the past five years I have tried lead-filtered seeds but find no definite clinical advantage and certain technical disadvantages.

The following is a résumé of the first case of cancer of the larynx treated with gold implants.

CASE II. June 12, 1925. Female, aged twenty-six. This patient developed hoarseness of a progressive character during the course of a first pregnancy. After delivery, it improved transiently but soon recurred. A clinical diagnosis of cancer was made by several laryngologists and laryngectomy advised. Section showed squamous cell carcinoma, predominantly Grade II (Fig. 5*b*). The patient and family, one of whom was a physician, flatly refused laryngectomy.

Examination showed a bulky papillary mass arising from the right cord and, as far as could be seen, replacing it entirely. It extended into the ventricle and to the anterior commissure but not beyond. It did not extend upward over

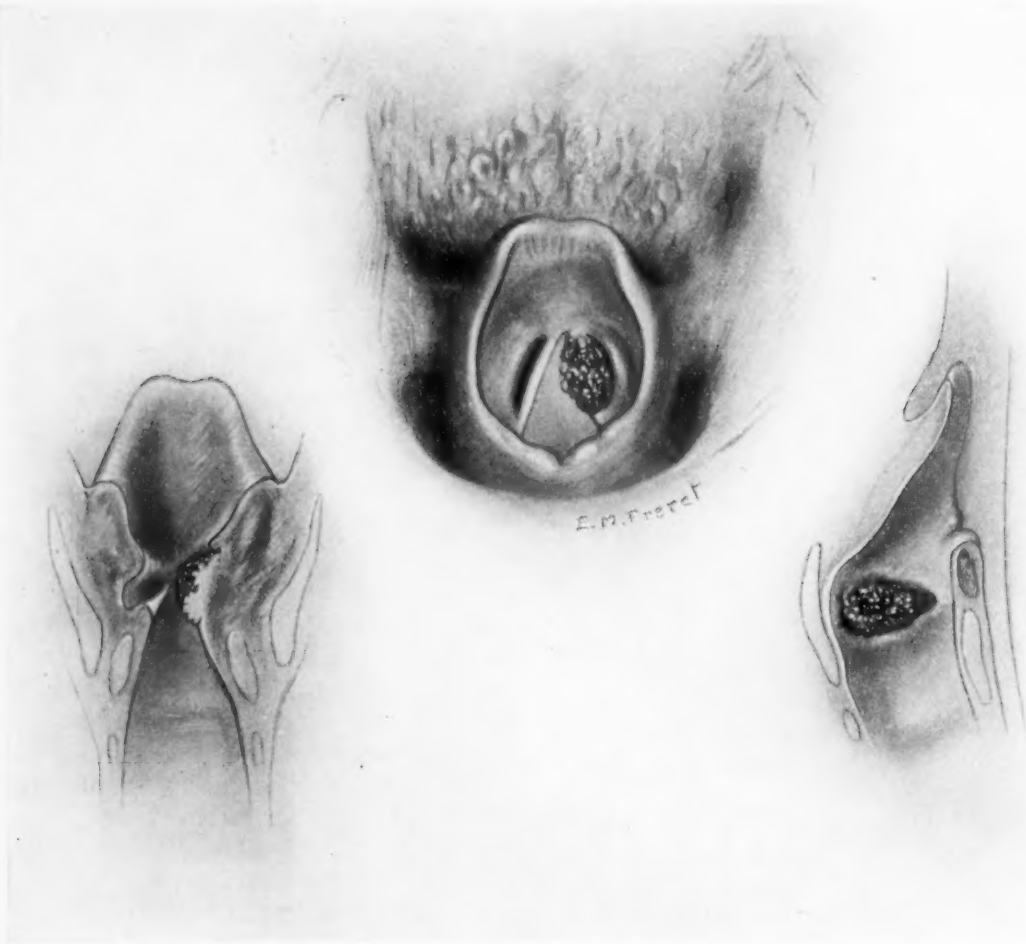


FIG. 5*a*. Case II. Gives a visualization of the extent of the growth.

the arytenoids (Fig. 5*a*). It did extend slightly below the cord. General health of the patient excellent.

Patient was treated by radium packs, 2 mm. brass plus 0.5 mm. silver filter and at 6 cm. distance, to each side of neck—10,000 mc-hr. to each side.

On June 17, 1925, radon seeds, 0.2 mm. gold filter, three in number and containing 2.55 mc. radon each were inserted into base of tumor through a direct laryngoscope—total dose 7.65 mc. (This was the first laryngeal case treated with gold filtered radon seeds.)

Patient remained in hospital three weeks, until immediate danger of laryngeal edema had passed. After three months there was no longer evidence of disease; all evidence of inflammatory reaction and feeling of irritability, however, did not subside for a year.

The patient was always nervous, temperamental and uncontrollable and at no time would she cooperate in saving her voice or reducing unnecessary strain on the larynx. The only cooperation, and that under some pressure, was the stay of three weeks in hospital when radon was implanted. (She has ignored appointments for follow-up examination for as long as three years at a time.) A second child was born without incident, three years after the original treatment, and a third two years later.

In March, 1934, she had some irritation and noticeable congestion about larynx and in June coughed up a gold seed. Irritation lessened. During the summer she indulged freely, against advice, in swimming and diving.

Late in August a questionable pelvic operation was done under a general inhalation anesthetic. About ten days later we were called upon to do an emergency tracheotomy. When the edema of the larynx had sufficiently regressed to permit of proper examination, no ulceration could be seen. Roentgenograms showed rarefaction of lateral alae of thyroid cartilage.

The inflammatory reaction subsided over a period of two months, leaving a stenosed glottis but at no time, nor since, was there secondary necrosis of tissue.

Later, repeated attempts were made to gradually dilate the glottic stenosis by direct and retrograde bougies but cooperation on the part of the patient was totally lacking. It was finally given up. Patient has a permanent tracheotomy. She has been free from cancer for over twelve years and has had normal voice for over eight years.

Fig. 5*b*. Case II. Photomicrograph showing the histopathology of the tumor.

Comment. Considering the age of patient and lack of cooperation, the result would seem to call for little, if any, apology, even though the individual gold seed values were too high. Life has been saved for twelve years and normal voice for eight years. The present condition is comparable, functionally, to that of laryngectomy. It need not have been so if patient had cooperated in reparative measures at the proper time. However, and in the light of interim experience, this is a case in which the present type of external therapy might reasonably be expected to both eradicate disease and save voice. Failure in this would not preclude thyrotomy and radon implantation, or localized use of the bipolar cutting cautery.

In the foregoing case it is also possible that the distribution of seeds may not have been most advantageous. Instrumentation through a direct laryngoscope is by monocular vision—not good at best. The seeds are inserted at a tangent to the surface of involvement. The depth of implantation cannot always be judged as nicely as might be expected.

In considering ways of improving this situation, I became impressed with the possibilities of utilizing the thyrotomy surgical exposure to render the growth directly

Fig. 6*a*. Case III. Gives a visualization of the extent of the growth.

accessible to inspection, palpation, and implantation at right angles to the surface of involvement. It has proved valuable in certain types of cases. In addition to a more accurate visualization, it permits of much safer localization of seeds relative to the cartilages.

The following is an example of one type in which it proved valuable, at least at that time.

Case III. August 11, 1926. Female, aged fifty-two. Patient had suffered from a chronic type of pulmonary tuberculosis for many years and periodic hoarseness was not taken seriously. After prolonged rest, disease in chest was arrested and hoarseness subsided. Hoarseness recurred and became progressively worse, later accompanied by dyspnea, and tracheotomy was done. No treatment, presumably because case was judged to be hopeless.

On admission a very bulky friable growth was found to be filling entire larynx, extending upward to level of arytenoids and downward to tracheotomy opening. Anatomic landmarks were largely obliterated by growth and edematous swelling of surrounding tissues (Fig. 6*a*). Section showed predominantly Grade II squamous cell carcinoma (Fig. 6*b*).

Roentgen therapy of a type which we would now regard as very indifferent was first given. Improvement, however, was pronounced. This was followed by laryngofissure and implantation of radon seeds, 0.2 mm. gold filter—11 mc. total. Wound was kept open because of local infection in tumor-bearing area.

In June, 1927, a node became palpable just lateral to the right ala of thyroid cartilage, and in July this was implanted with radon seeds, 0.3 mm. gold filter—total 13.2 mc. Biopsy from the node showed it to be of the same histologic structure as primary growth.

By the end of August all evidence of growth had subsided and patient was able to get on

comfortably without dressing in wound, or tracheotomy tube.

A pronounced stricture was present above, however, and in view of the chronic pulmonary tuberculosis, it was not considered wise to resort to further surgery in an effort to relieve this, in the hope of being able to close the thyrotomy opening. Patient has remained free from disease now for ten years.

Comment. In the light of interim experience, it would seem that the surgery, intensity of local reaction, and prolonged dressings could have been avoided by the present method of external therapy. It is doubtful, however, if the tracheotomy tube, present for many months before admission, could have been dispensed with because of stenosis at level of the glottis. It is also doubtful if the metastatic node would have been eradicated without direct surgical exposure and radon implantation.

The following is an example of the type of advanced case which I consider suitable for laryngofissure, under present standards —one with unquestioned cartilage involvement on admission.

Case iv. December 1, 1926. Female, aged twenty-two. History began with hoarseness following a severe cold in 1925 with dyspnea developing in July, 1926. Tracheotomy done in August, 1926. No treatment.

In December, 1926, the entire larynx was found to be filled by a mass of granular vascular tumor tissue with a great deal of edema; no definite landmarks other than epiglottis discernible by indirect laryngoscopy and no air way. Tracheotomy sinus lined by tumor and fungating tumor surrounding opening at skin surface (Fig. 7*a*).

Sections showed considerable variation in histology; in places, infiltrating Grade I squamous cell carcinoma, while at other points Grades II and III predominated (Fig. 7*b*).

Treatment during the first three days was by radium trays, 2 mm. brass plus 0.5 silver filter, at 3 cm. distance, to both sides of larynx—total dose 12,000 mc-hr.

On December 13, 1926, thyrotomy with cautery removal of considerable tumor, and implantation of radon seeds, 0.3 mm. gold filter—total dose 21 mc. Wound packed open. The

Fig. 6*b*. Case III. Photomicrograph showing the histopathology of the growth.

disease had involved cartilages, isthmus of thyroid and underlying tracheal wall.

Eight days later a similar total dose of radon seeds was implanted in the open wound.

In January, 1927, radon seeds, same filtration, 2.5 mc. total, were implanted in a nodule at the border of the surgical wound.

The reaction was very severe but by fall had healed completely and patient was at work. Stenosis complete and tracheotomy permanent. Patient now free from disease for ten years.

Comment. The end-result is that of total laryngectomy but in a case in which the usual total laryngectomy would have been impossible and unsuccessful because of the extent of disease. It is a good example of the value of laryngofissure as an operation for exposure and access as well as drainage in an advanced case with cartilage involvement and where a part of the tumor, at least, was known to be histologically radioresistant. The local intensity of radium dosage and total recovery period could have been reduced by preliminary external irradiation by present methods.

Next is an example of another of the gold seed implantation cases, where, after a seemingly perfect result for six years, an error was made in resorting to roentgen therapy instead of a thyrotomy plus one of two possible local measures.

FIG. 7*a*. Case IV. Drawings showing the growth distribution.

CASE V. December 3, 1926. Male, aged fifty-two. Hoarseness developed during the summer of 1926 and gradually increased in intensity. No impairment in general health of the patient.

The anterior two-thirds of the left vocal cord was found to be involved by a flat, non-bulky new growth, centrally ulcerated. Infiltration extended around anterior commissure to end of right cord. Above the left cord, the infiltration extended slightly into the floor of the ventricle and only for a short distance below the cord level (Fig. 8*a*).

Section showed an infiltrating squamous cell carcinoma, predominantly Grade II (Fig. 8*b*).

Treatment was by radium packs, 2 mm. brass plus 0.5 mm. silver filter at 6 cm. distance, to each side of neck, for a total dose of 20,000 mc-hr. This was followed by implantation of radon seeds 0.3 mm. gold filter—total dose 5 mc.—through a direct laryngoscope.

Five months later there was no evidence of remaining growth, very slight evidence of scar tissue, and patient had a good voice. Conditions remained thus for six years; patient used his voice very freely and at times spoke over the radio. He also persisted in smoking.

Early in 1933 a small eroded area was noted on the left cord immediately back of the point to which growth had extended originally. Under local medical treatment this seemed to improve, but only transiently, and soon it was evident that there was a recurrence of growth.

Secondary necrosis from further implantation of radon was feared and a desire to avoid thyrotomy led to a decision to employ high voltage roentgen therapy. As subsequent events indicate, this was the point of error in judgment. I believe the superficial localized area of recurrence could have been eradicated by radon implanation, without necrosis. Certainly thy-

rotomy and bipolar cutting cautery removal would have eliminated it with a minimum defect, leaving a patent air way and a low-pitched hoarse voice.

The high voltage roentgen therapy was at 200 kv., 50 cm. skin-target distance, 0.75 mm. Cu plus Al filter, 5 cm. circular field, 400 r measured in air, daily exposure. Exposures alternated from one side of neck to the other in the beginning; later 200 r to each side daily. The rate of delivery, however, was rapid—more than 20 r per minute.

A very definite reaction in throat was noted at 1,600 r to each side. Over a two-month period a total dose of 9,000 r was given with these factors.

After another two months the larynx seemed once more to be in excellent condition and with no evidence of disease. It continued so for another five months when, following a severe cold, edema appeared over the arytenoids, persisted,

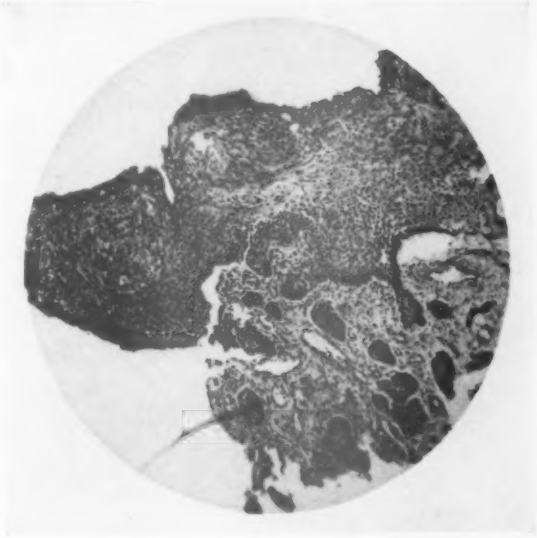


Fig. 7*b*. Case iv. Photomicrograph showing the histopathology of the growth.

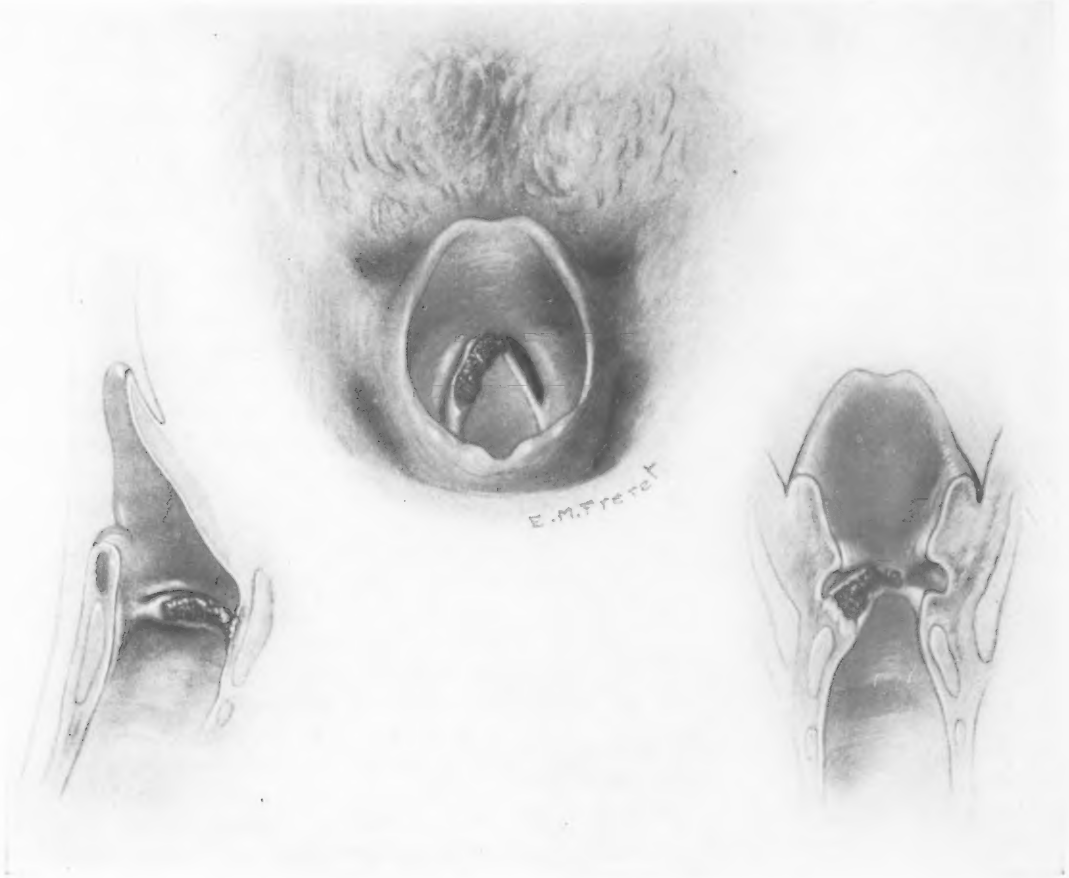


Fig. 8*a*. Case v. Shows the original growth distribution.

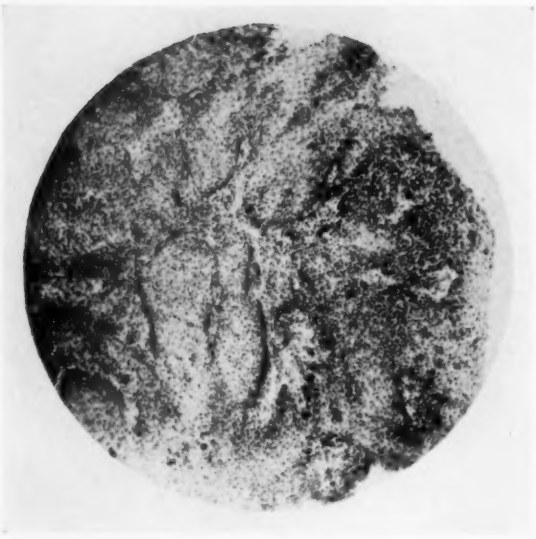


FIG. 8*b*. Case v. Photomicrograph showing the characteristic histopathology.

and gradually extended to the pyriform sinuses.

A fortnight of hospital care appeared to be beneficial when acute edema developed, necessitating emergency tracheotomy. A fortnight later median laryngotomy was done. Thyroid cartilages were found practically stripped free from muscular and tendinous attachments and bathed in serous inflammatory exudate. The cartilage was of the consistency of soft leather. The interior of the larynx showed a great deal of secondary necrosis of soft parts. All debris and as much of cartilages as possible was removed and wound packed wide open. Postnasal feeding tube was employed to care for patient's nutrition. During the next two months the wound cleaned up and healed. Histologic examination of all tissues removed failed to show remaining growth. A small plastic operation was done to finally close off the hypopharynx.

There has been no further evidence of growth in the intervening three and a half years. The patient, in excellent general health, carries on in a busy executive position, and uses an artificial speaking instrument with unusual facility.

Comment. This case shows very clearly the hazard of attempting intensive roentgen therapy in a larynx which has received previous irradiation—even though it was several years before. The factors of irradiation I realize were not the best.

The case originally was not suitable for thyrotomy or hemilaryngectomy because of the involvement of the anterior end of the second cord. It was suitable, however, for total laryngectomy and the end-result is exactly that of total laryngectomy. Still, the patient feels very strongly that retention of perfect voice for an added six years well warranted the course followed.

My own criticism rests on the error in judgment in not resorting to thyrotomy and further radon implants, with or without cautery, instead of using intensive roentgen therapy.

The next case is one illustrating the need for most careful observation of even the initial response to external irradiation and, beyond that, what may be attained by close combination or cooperation between irradiation and the less extensive operative procedures. The aesthetic as well as ultimate functional result, for the period of treatment (eight years ago) might also be mentioned.

CASE VI. July 15, 1929. Female, aged twenty. At the age of twelve years a papilloma developed on the right cord anteriorly, was removed several times and in various ways. A web formed in the anterior commissure.

Six years ago this was removed in Vienna and a metal plate fixed in the anterior commissure by a wire brought out through the midline to hold it firmly in place, thereby preventing the formation of the web. This plate sloughed out through the front, one month later. Wound soon healed and voice remained clear for five years.

Hoarseness developed and became steadily worse over a six-month period during which frequent silver nitrate applications were made. For six weeks swelling has been noted in the right cord, beginning in the midportion, and rapidly extending until, on admission, the entire right cord, anterior commissure and anterior half of left cord were involved by a fairly bulky growth, centrally ulcerating and extending about 1 cm. below the right cord (Fig. 9*a*).

Section showed squamous cell carcinoma, predominantly Grade II, infiltrating and suggestively radioresistant (Fig. 9*b*).

Roentgen therapy was begun but before well

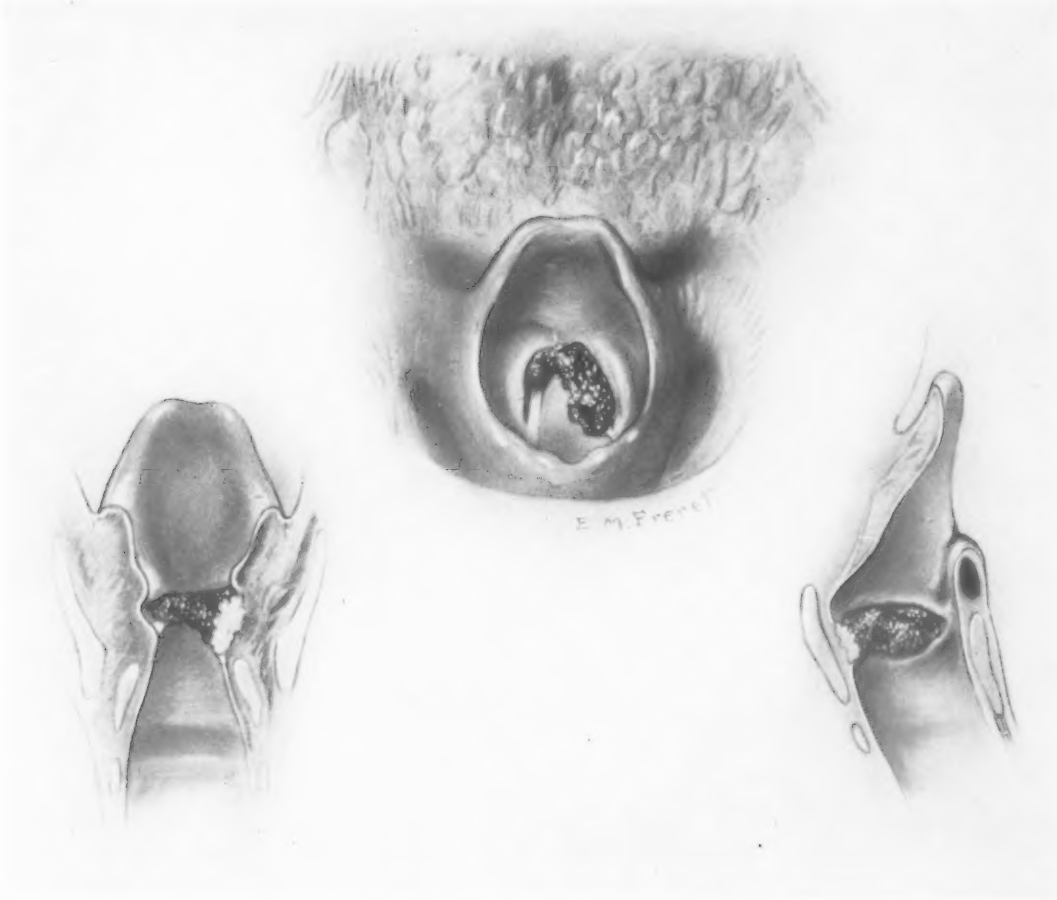


Fig. 9*a*. Case vi. Visualizes the extent of the growth.

under way it was decided to switch to radon implants because of the histologic suggestion of radioresistance. (There was already a noticeable regression from 1,000 r in air with the same factors as given in detail in Case v.) We now know that this initial response means more, clinically, than the suggestion of radioresistance indicated by the histologic slide.

A week later, July 31, 1929, radon seeds, 0.3 mm. gold filter, seven in number and 2.16 mc. each, were implanted through a direct laryngoscope—total dose 15.12 mc.

The patient was unusually cooperative and refrained completely from using the voice. Reaction was severe, but at the end of three months had entirely subsided, patient was comfortable and there was no evidence of disease. There has been no further growth.

However, after another three months the scar became irritable and two months later, following a severe cold, secondary necrosis

Fig. 9*b*. Case vi. Photomicrograph showing the histopathology as far as a single field will permit.

developed. This necessitated tracheotomy, laryngofissure, removal of debris and infected cartilage. After four months patient left hospital with clean laryngofissure wound but lacking cartilaginous support, and with tracheotomy tube.

The patient has been free from cancer for eight years.

Comment. The switching of a plan of action, once decided upon after due consideration, is rarely good practice. In this

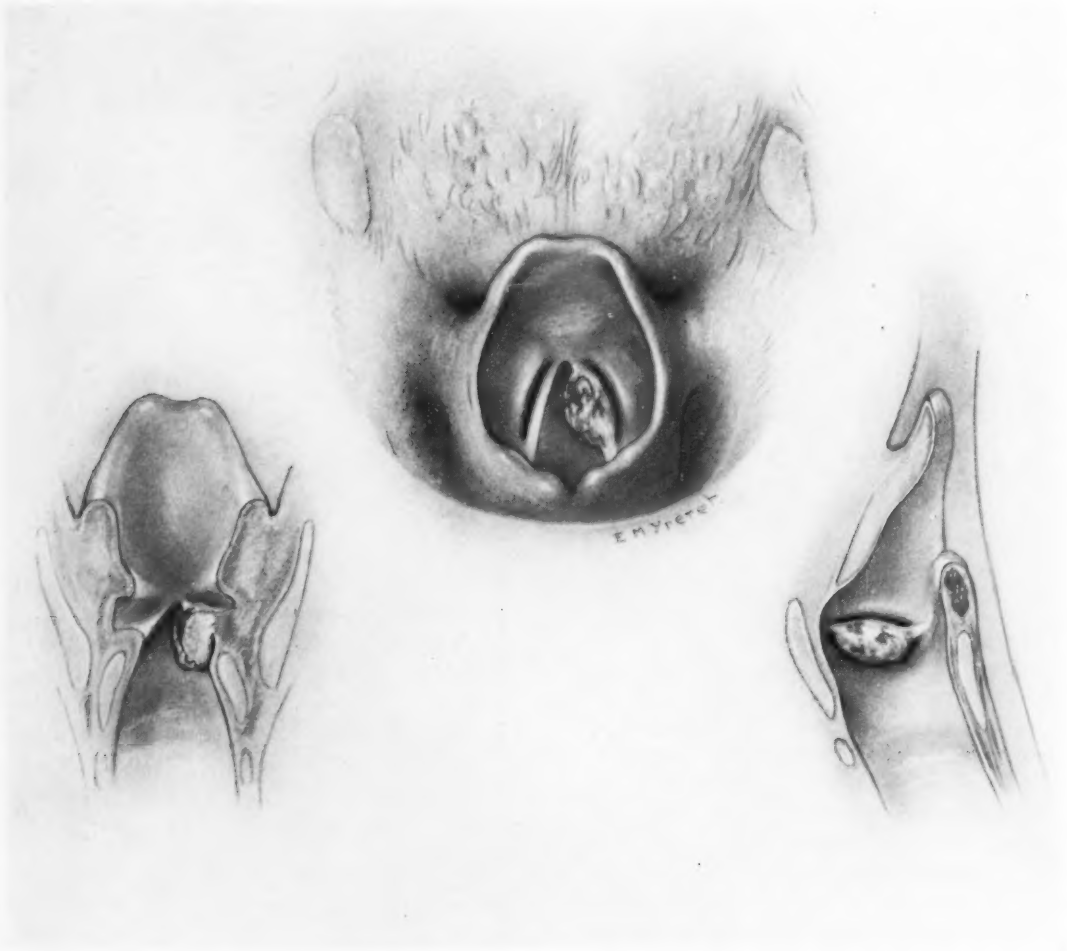


Fig. 10*a*. Case vii. This is a visualization of the growth extension. Note freedom of anterior commissure and posterior end of cord.

After two years, the supraglottic stricture was gradually dilated with retrograde dilators. A series of plastic operations was done with lined flaps, strengthened by cartilaginous stays grafted between the two layers of the flaps. In this manner, an air way was reconstructed so that the patient might breathe normally and have a low-pitched voice comparable to that which obtains after thyrotomy and hemilaryngectomy. This was finally completed eight months ago.

instance, the initial prompt response to a small amount of roentgen therapy should have outweighed the doubt raised by the histologic report of radioresistance. Next, the radium dosage was too heavy; seven seeds were necessary for proper distribution but the individual values were unnecessarily high.

The ultimate saving of life and functional result is due to prompt resort to

surgery and is now better than an original laryngectomy. This is important in an attractive young woman. The reconstruction, however, would not have been possible had it not been for her marvelous cooperation.

Next is an example of the type of case in which thyrotomy and local removal are entirely justified if the surgeon be so minded. In this I am thoroughly in accord with MacKenty and most laryngeal surgeons that partial removal of underlying cartilage is not good practice. It leaves no barrier to outward extension of growth into the extralaryngeal soft tissues if recurrence develops.

Case vii. December 16, 1930. Male, aged forty-five. History of progressive hoarseness over a period of a year. No dyspnea or other symptoms.

Local examination revealed a growth with broad base arising from border and under surface of right vocal cord, rather bulky and papillary, with surface of a whitish, leathery appearance suggestive of pachydermia laryngis. No extension into either anterior commissure or arytenoid (Fig. 10*a*).

Section showed hornifying papillary squamous cell carcinoma, Grade 1, and of low relative malignancy (Fig. 10*b*).

A low tracheotomy and thyrotomy with bipolar cutting cautery removal of growth, right cord and ventricular band was done. Tube was removed after the second day and healing was complete within less than a month. Histologic examination of specimen suggested complete gross removal of tissue.

On account of questionable postoperative thickening still persistent on the right side after three months, some roentgen therapy was given. Using the factors stated in Case v, 1,600 r was given to each side, but over a three-month period.

Patient has been free from disease for over six and a half years and has a low-pitched hoarse voice which has not improved after the first year and a half.

Comment. Case iv represented an extremely advanced case in which thyrotomy was a distinct aid to drainage and access. This case is an example at the other end of the scale suitable for cure by thyrotomy and local removal.

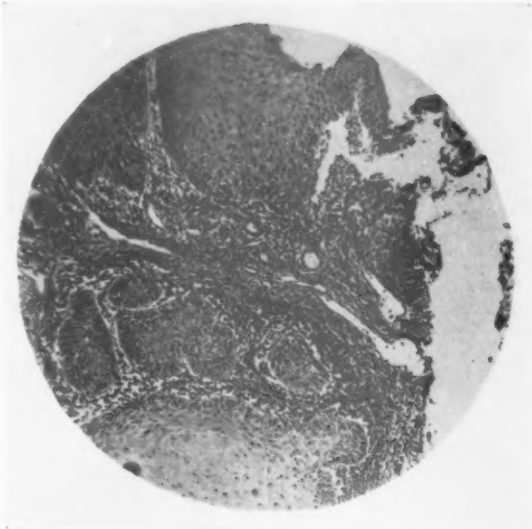


Fig. 10*b*. Case vii. Photomicrograph showing the histopathology of the growth.

The postoperative therapy was, I believe, poorly conceived and executed, and of very doubtful value. With present technique, however, I do not believe the thyrotomy would be justifiable until at least a full course of intensive roentgen therapy had been given. An effort to save the normal voice would certainly warrant it, might well be successful, and would not seriously complicate the subsequent doing of thyrotomy if ultimately judged necessary.

The exposure by thyrotomy or laryngofissure for access and radon implantation or drainage, as well as occasional local removal, had served varied and useful purposes, as I hope the previous case reports have indicated. It extended the scope of both life saving and conservation of function—the latter, however, not as much as the former.

The trend toward more high voltage roentgen therapy was definitely indicated. The basic principles of Coutard were before us, yet not fully appreciated in their entirety.

The following case reports are being given to illustrate the benefits derived by improving one factor after another. Beyond that, it is hoped they will show something of the individual problems which

center around each case—problems which can only be met by the most careful observation of the patient from day to day under treatment.

The physicists have given us tremendous aid in so many directions by means of which we are enabled to safeguard normal tissues, deliver to the tumor-bearing area a desired quality of radiation most economically, and calculate the total physical quantity and relative effect from a given set of treatment factors at any one time. For all of this and much more we are indebted to many enthusiastic workers, but chiefly to Mrs. Quimby and her associates, under the able guidance of Failla.

The tumor pathologists have aided us by their interpretation of the histology of the untreated tumor, thereby assisting in selection of a most desirable treatment combination in the individual case, and, by a study of the tumor under treatment, have aided at times in appraising the relative effectiveness of that treatment. The biopsy specimen, however, is of necessity small and this is particularly true when taken from the larynx. We cannot expect that the specimen, or even specimens, will give us the entire histologic picture throughout the entire tumor. To base all therapy or explain all results by the histopathology is fallacy.

The biophysicists have aided us also in our clinical work by offering explanatory

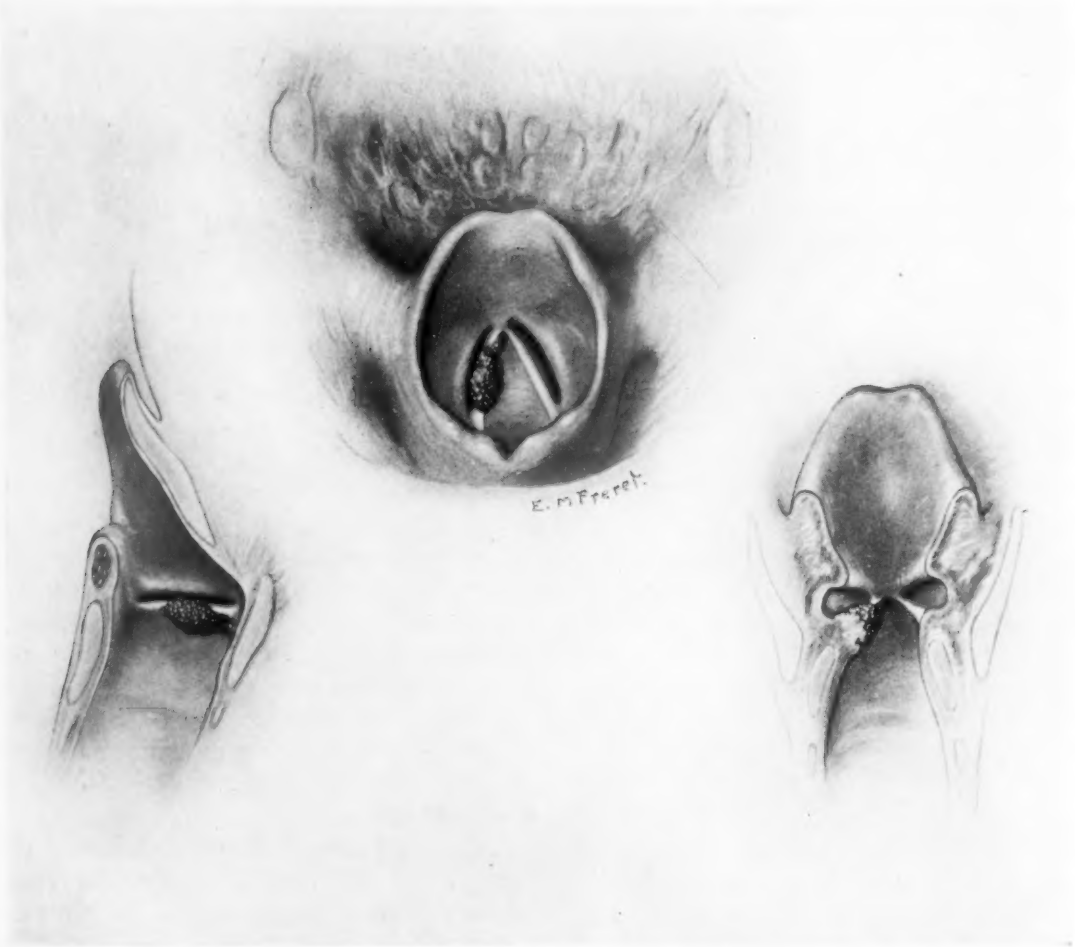


FIG. 11*a*. Case VIII. The extent of the tumor is indicated.

evidence for many phenomena which formerly were entirely a matter of conjecture.

With all of this assistance from various sources, we must still remember that we as clinicians must practice clinical medicine with careful attention to detail in the individual case, and with the same type of observation of the patient exhibited by the pioneers in clinical medicine, who did not have the various laboratories available.

Many of our cancer problems are still unsolved. We have not yet reached the point where the laboratory and the microscope tell us just what to do, leaving us in the position of animated robots to put it into effect. This I make bold to say with all due respect for our associates in the laboratories. For their work and assistance no one has a keener appreciation than I.

The laryngeal cancer field is especially one in which all of the more exact sources of information and explanation fail at times to indicate just why certain things happen.

The following record may serve to indicate what I wish to convey.

Case VIII. December 15, 1930. Male, aged forty. The patient had noted progressive hoarseness for three and a half months, and two weeks before consultation, biopsy had been done.

Examination revealed a localized but bulky growth arising from the under surface of left cord in its anterior half, extending slightly beyond the midline subglottically but not into the anterior commissure proper. That is, the anterior end of the right cord was not involved. The laryngeal cartilages were not fixed. General health of patient excellent (Fig. 11*a*).

The section showed squamous cell carcinoma, predominantly Grade II (Fig. 11*b*).

Treatment was with 200 kv. roentgen therapy, 50 cm. skin-target distance, 5 cm. circular field, 0.75 mm. Cu plus 1 mm. Al filter, 250 r measured in air, per individual exposure, at a rate slightly above 20 r per minute. Exposures alternated from one side of neck to the other and usually only two treatments per week, occasionally three. Over an eight-week period, 1,500 r was thus given to each side of neck.

At the end of two weeks (500 r to each side) there was noticeable tumor regression, and mild local inflammation in the normal tissues immediately surrounding. At the end of eight weeks there was no evidence of remaining tumor nor has there been any recurrence in the interim of over six and a half years. At no time was there complaint of dry throat.

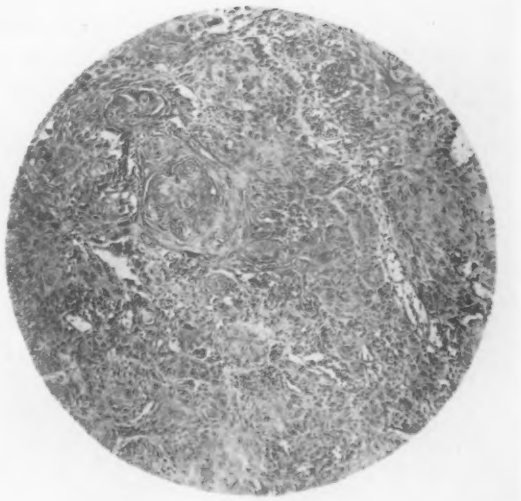


Fig. 11*b*. Case VIII. Photomicrograph showing an average microscopic field.

Comment. This case is most unusual and I have no duplicate. It will undoubtedly raise the question of error. The peculiarly prompt response, not only in the tumor, but in the surrounding mucosa, led to rechecking of the treatment machine by a physicist of unquestionable competence; the measurements were correct. No filters were omitted.

The section has been repeatedly reviewed, with nothing in the histology or error in diagnosis to account for the result. The question of possible mixing of biopsy specimens has been proved to our satisfaction to have been impossible. The biopsy itself did not constitute a complete local removal.

The factors of irradiation and spacing of individual exposures are recognized as being very poor indeed. When the normal tissue recovery rate is calculated, it makes the ultimate dose all the more fantastic. There was nothing unusual in the gross anatomy of the patient's neck—he wore a size 15 collar.

The end-result—six and a half years later—simply shows that response beyond the ken of histologic interpretation, qualitative and quantitative physical calculation does occur.

If the patient is carefully watched clinically from day to day, under treatment, the rate of early response is easily noted.

The short duration of symptoms in an observing patient, and apparently rapid rate of growth are also worthy of note. They usually suggest the probability of ultimate response to a total irradiation in the lower brackets.

The following is a case which showed an unusually sharp reaction from the total amount given and with the factors used.

CASE IX. June 21, 1933. Male, aged sixty-five. About ten years ago, the patient had a severe throat infection followed by loss of voice which cleared up after two months of treatment, but recurred transiently at intervals. Ten weeks before consultation, hoarseness recurred and has become progressively worse.

Examination revealed a circumscribed but bulky ulcerating growth involving the midportion of right cord. It extended below the cord but not into the anterior commissure. No suggested involvement of cartilage (Fig. 12*a*).

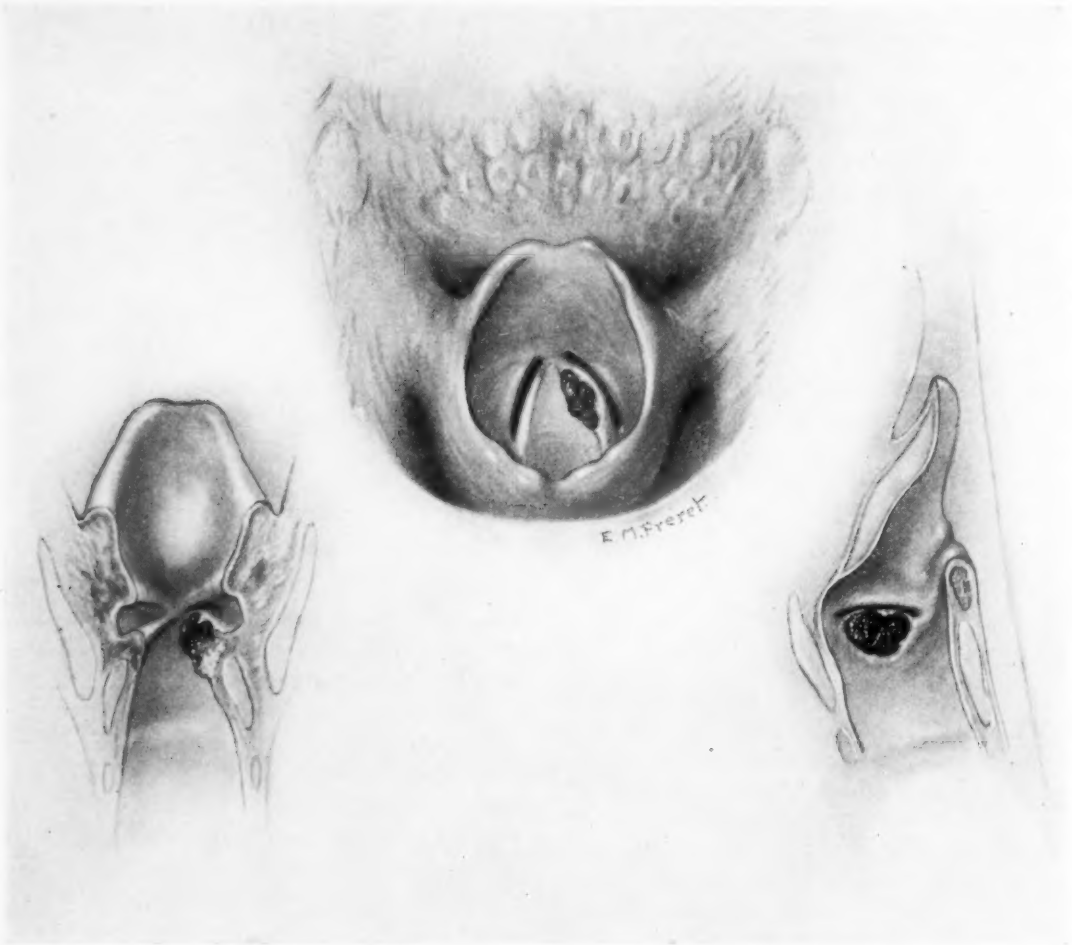


FIG. 12*a*. Case IX. Gives the extent of the growth.

Section showed a squamous cell carcinoma, predominantly Grade II, but with some areas more anaplastic (Fig. 12*b*).

Treatment was by roentgen therapy at 200 kv., 50 cm. skin-target distance, 5 cm. circular field, 0.75 Cu plus 1 mm. Al filter, 175 r measured in air, per individual field, at 20 r per min-

ute, to each side of neck, daily, five days per week.

At the end of a fortnight there was no skin change but mucous membrane reaction was noticeable and the growth was receding.

At three weeks the mass was much reduced, skin reaction beginning and throat congested, uncomfortable and very dry.

Three days later all symptoms were aggravated and progressed so rapidly up to the end of the fourth week that the patient was hospitalized for better nursing care, especially from the standpoint of feeding. After two weeks of such care, all local symptoms had regressed, general condition was again stabilized, and, while no evidence of growth remained, it was decided to proceed with irradiation.

The decision, however, to treat or not on any given day, was based on local appearance and symptoms incident to the previous day's treatment. On this basis, patient had received, at the end of fifty-three days, a total of 3,750 r to each side—7,500 r in all. This is substantially less than many tolerate with less of local symptoms, providing their throat is kept clean and well oiled.

There was no evidence of growth and no acute reaction. No aggravating symptom except dryness. No further treatment given. The dryness was very annoying for a year and then gradually faded out. Patient has now been free from all evidence of growth for over four years and has a perfectly normal and comfortable voice and throat.

Comment. This case was ideal for either thyrotomy and local removal or total laryngectomy, depending on the attitude of the individual laryngeal surgeon. The case which is ideal for such surgery is usually ideal for irradiation as well. From the latter standpoint, the result is not unusual. The treatment represents perhaps a bit better than the average met with in routine practice.

Attention is called to division of the daily dose to each side of the neck rather than alternate sides on alternate days, to the acuity of symptoms relative to total dose with low filtration and relatively high r per minute and per day, and to the distressing dryness which persisted beyond a year with these factors. Daily general care of the throat and prompt hospitalization to maintain a good general state of nutrition is also worthy of note.

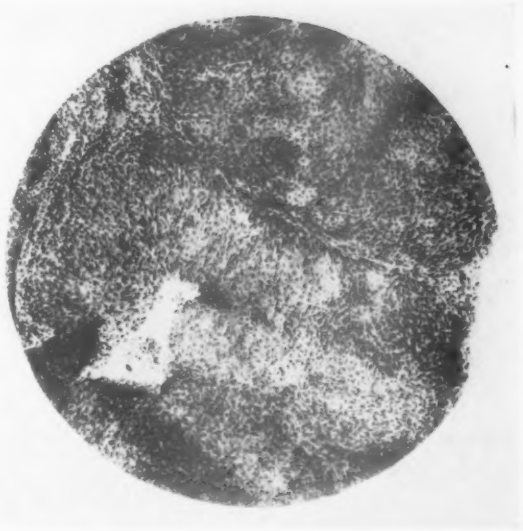


Fig. 12*b*. Case ix. Photomicrograph showing the histopathology of the growth.

The next case is an excellent one for comparison with the former (Case ix).

Case x. June 12, 1933. Male, aged forty. Transient but persistent hoarseness had been present in this case for two years before consultation but had been progressively worse for three months immediately preceding. He was a very heavy cigarette smoker—this was stopped.

Examination showed an ulcerating growth involving mid and anterior two-thirds of left cord. It extended into the ventricular fold, very little below the cord, and to, but not into, the anterior commissure (Fig. 13*a*).

Section showed squamous cell carcinoma predominantly Grade ii, but with more anaplastic areas noticeable in places (Fig. 13*b*).

It will be noted that this case resembles Case ix very closely, both anatomically and histologically and, from the dates, that their treatment ran practically concurrently. The factors, intensity and spacing were exactly the same in the beginning. The size of necks was the same and both had dark skins. Treatment was with the same therapy machine.

In this case the individual exposures were reduced to three per week after the third week. At no time was the local intensity within the larynx as severe as in the former case and at no

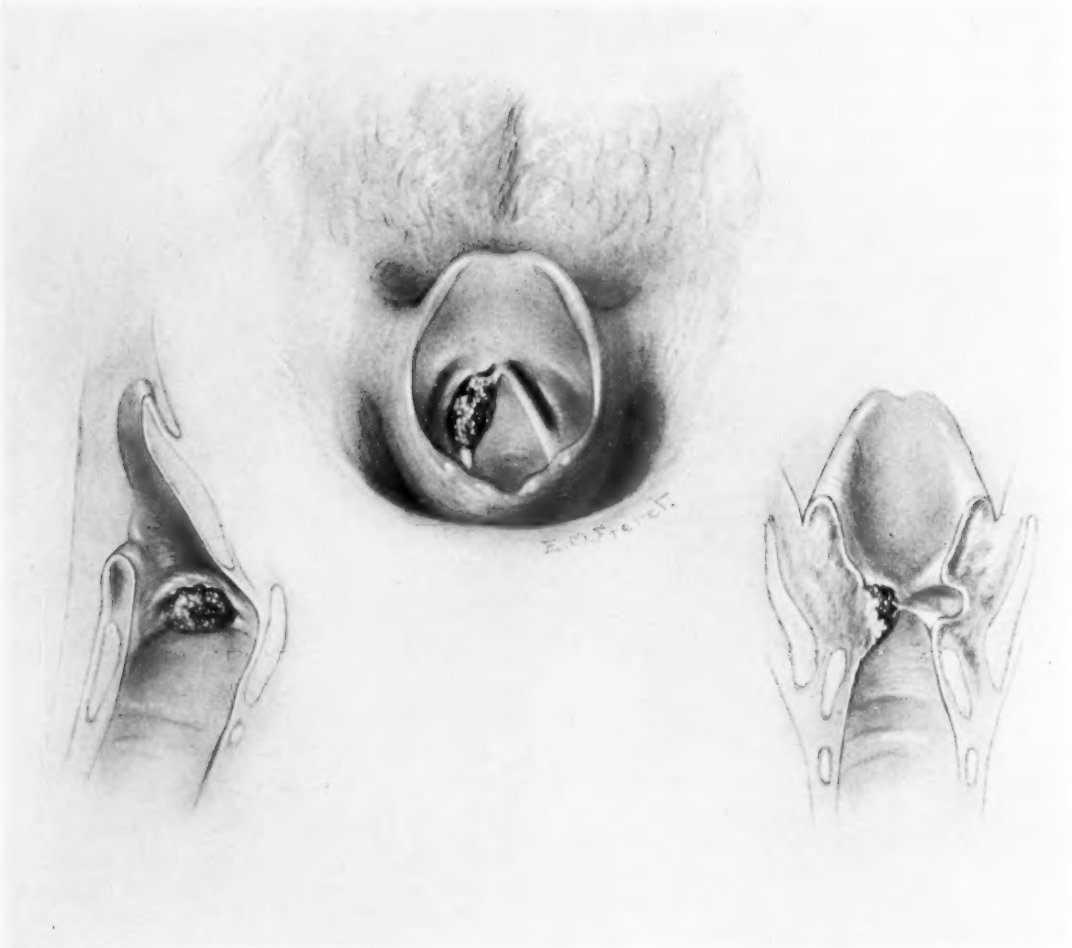


Fig. 13*a*. Case x. Indicates the extent of the growth.

Fig. 13*b*. Case x. Photomicrograph showing the histopathology of the growth.

time was there need for hospitalization. At the end of fifty-three days (total treatment period of Case ix), the total dosage was the same and there was no evidence of growth. Calculation of variation in ultimate total dose from dates of exposures and normal tissue recovery rate showed that they are practically equal in intensity.

Treatment was continued, however, on each day, up to seventy-seven days, that local condition and symptoms warranted. The ultimate dose was 4,500 r to each side—9,000 r total.

Dryness of the throat cleared up somewhat more quickly in this case than in the former. The patient has been free from growth for over four years, with normal voice. He does have, however, noticeable congestion about the arytenoids and ventricular folds during periods of unusual humidity or when he has been in a heavily smoke-laden atmosphere for any length of time.

Comment. Comparison of this case with Case IX indicates an appreciable difference in individual tolerance and strongly suggests that, with the factors used, 350 r per day is probably excessive. Both cases indicate that the quality of radiation produced by these factors has definite quantitative limitations which do not obtain at the same level with a better quality of radiation.

The next report shows the response of a very early and superficial type of growth, even though fully differentiated, to a quality of irradiation comparable with or only slightly better than that in general use.

Case XI. July 10, 1934. Male, aged forty-nine. The history is of hoarseness, progressive over a period of ten months, first noted following a very severe cold.

Examination revealed a congestion of both cords with peculiar thickening of left cord and superficial ulceration involving anterior two-thirds, extending around anterior commissure and involving anterior half of right cord. Very little extension away from either cord (Fig. 14*a*).

Section showed fully developed squamous cell carcinoma, Grade I, not deeply infiltrating, but of radioresistant type (Fig. 14*b*).

The treatment was by roentgen therapy using the same factors as in the two previous cases except that the daily dose was limited to 150 r to each side. After 1,500 r had been given to each side, there was a noticeable general reaction within the larynx and definite growth regression.

Exposures were limited to 100 r to each side daily. At 2,500 r total to each side, there was definite skin reaction but no desquamation. Reaction within the larynx was sharp but in no way uncomfortable—no irritation on swallowing, no excessive mucus, no edema, no dryness, and voice was better.

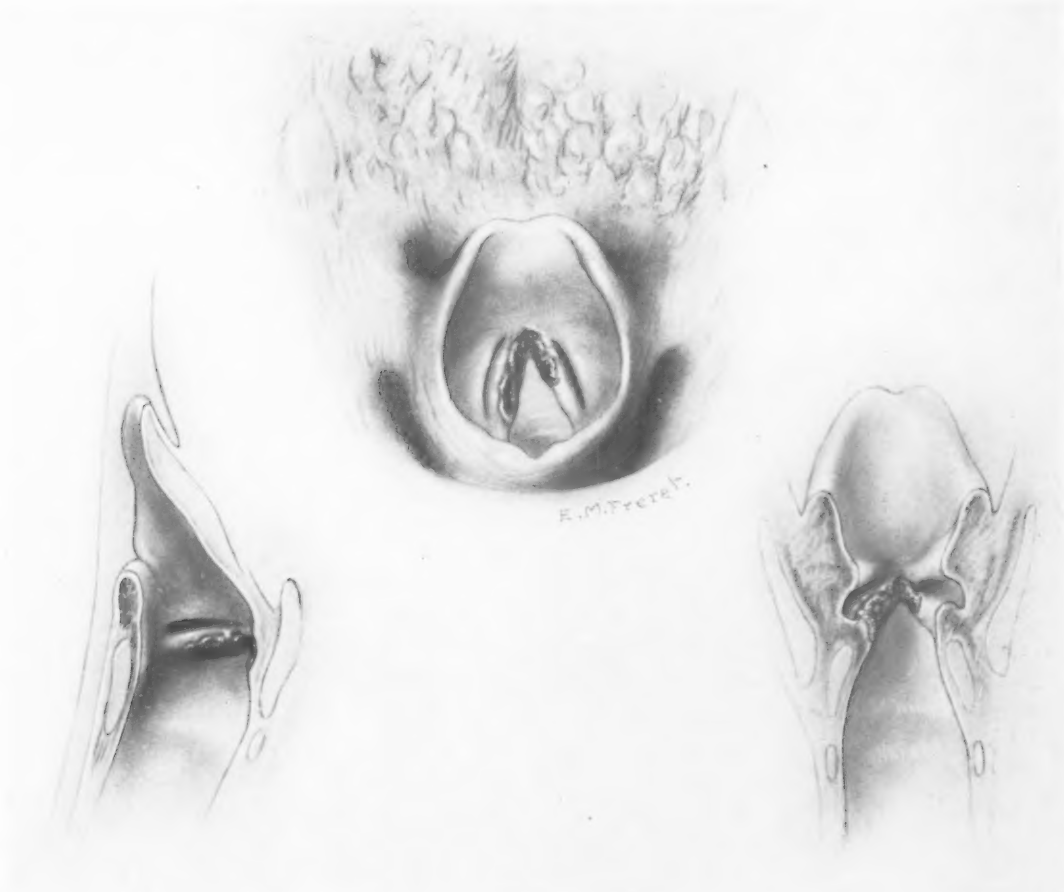


Fig. 14*a*. Case XI. The extent of the growth is visualized.

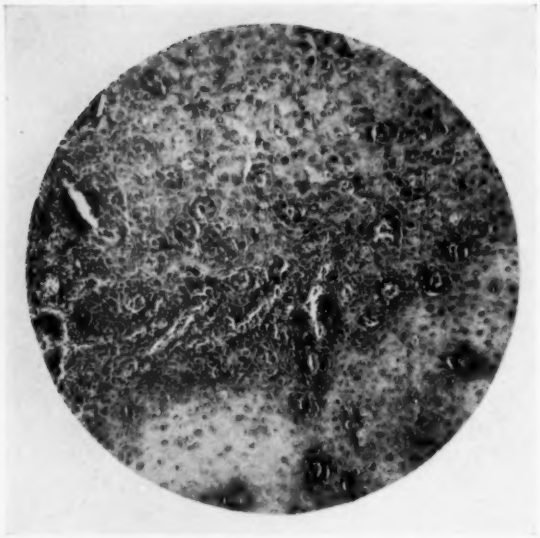


FIG. 14*b*. Case XI. Photomicrograph showing the histopathology of the growth.

The line of exposure was shifted to a single field of the same size directly through from before backward—150 r daily. This was carried up to 2,500 r over this area. Total elapsed time fifty-eight days and total dose 7,500 r.

At this point there was a uniform exudate over interior of larynx and patient was annoyed by morning cough from tenacious exudate. The skin was in good condition all around and there was no suggestion of remaining growth. Irradiation was stopped. It seemed that we had reached a favorable point for a superficial growth without doing appreciable damage to any of the normal structures.

Two months later, there was no evidence of growth, no irritation within the larynx, no dryness, no skin changes other than epilation of beard, and the patient stated that his voice was entirely normal. It has remained so for the intervening three years.

Comment. The case was ideal for laryngectomy—but also for irradiation.

With the factors employed in these last three examples, it would seem that 7,500 r total in two months represents a safe limit, if no gross damage to normal structures is an objective.

Varying the daily exposure by daily observation, and utilizing the third area, permits of carrying the individual case through without gross damage to normal structures. The anterior field seems especially desirable with growth in the anterior commissure.

For a superficial growth—but only for a superficial growth—it would seem that these factors are reasonably safe. They are certainly more economical than what I have chosen to refer to as a "better quality" of radiation.

The final case report indicates what I regard as nearest to the ideal result in my personal experience with laryngeal cancer to date.

CASE XII. July 13, 1936. Male, aged fifty-eight. Patient had noted a tickling sensation in throat for three years but attributed it, probably correctly, to cigarette smoking. For many years he had used from 80 to 100 cigarettes daily, and at times used an excess of alcohol. Two years before, and during an alcoholic period, his blood pressure averaged 220/150. Six months before consultation an attack of influenza was followed by definite hoarseness which persisted, and continued in aggravated form after a second influenzal attack three months later. After the second attack, cigarettes were reduced to 40 per day. In spite of his excesses his general appearance was excellent.

Examination showed an ulcerating growth involving the anterior three-fourths of the left vocal cord and into the anterior commissure. It extended below the cord and upward into the ventricle and on to the ventricular fold. Mobility was sharply limited but not fixed. The throat was extremely difficult to examine on account of the prolonged excessive use of tobacco and alcohol (Fig. 15*a*).

Section showed squamous cell carcinoma, Grade II, infiltrating and only moderately radiosensitive (Fig. 15*b*).

Treatment was by roentgen therapy at 200 kv., 80 cm. skin-target distance, 4×5 cm. rectangular field, filter Thoraeus plus the copper of the ionization chamber in the master-cone, making a total filtration equivalent to 2.32 mm. copper. The rate of dosage delivery was 6.75 r per minute, measured in air. Two lateral and one anterior field were used—three in all (Fig. 15*c*). Treatment over each field daily for five days per week. The first day 50 r only was given over each lateral field. For the following week, 75 r per field daily. Thereafter 100 r per field

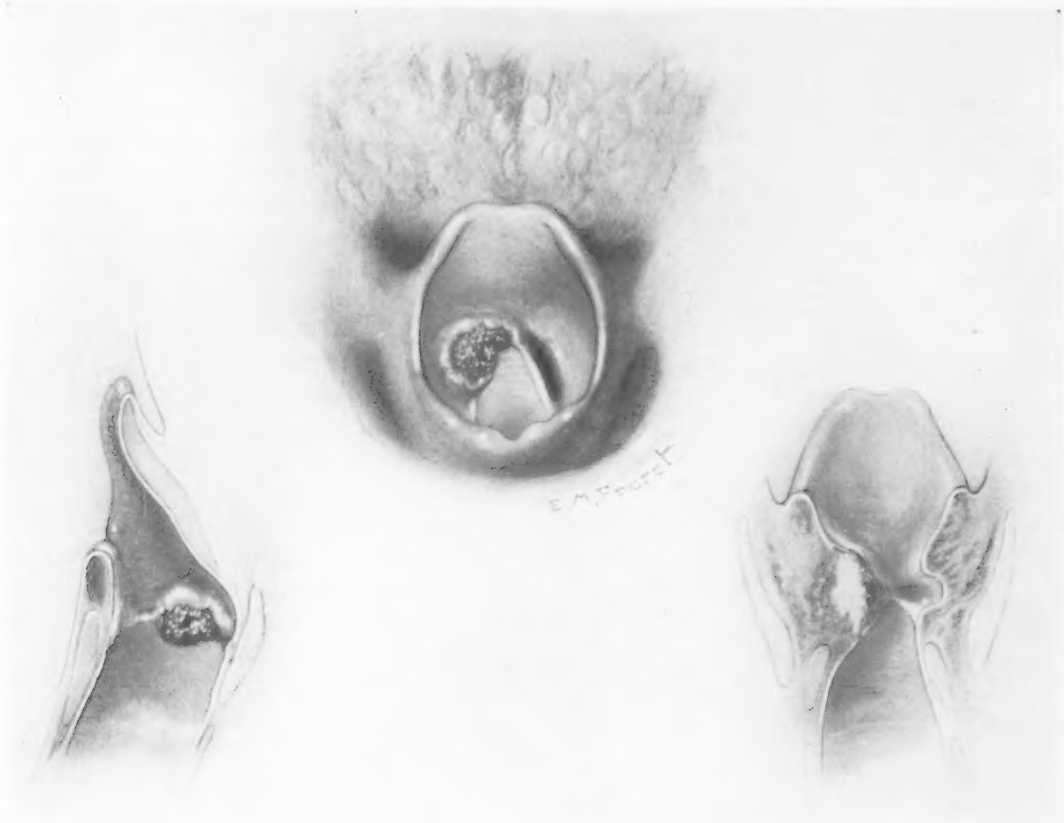


Fig. 15*a*. Case xii. Visualizes the extent of the growth.

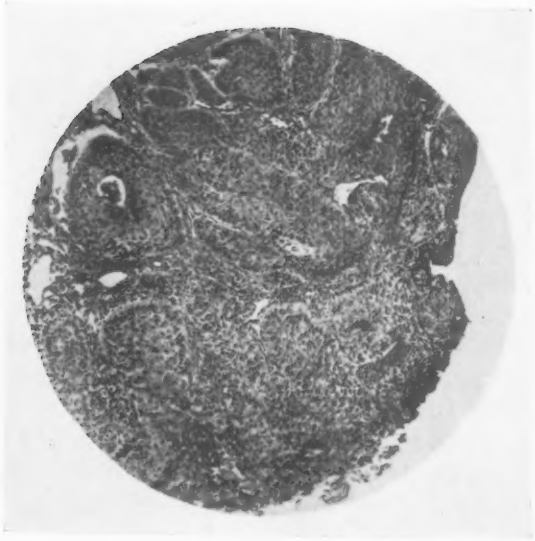


Fig. 15*b*. Case xii. Photomicrograph showing the histopathology of the growth.

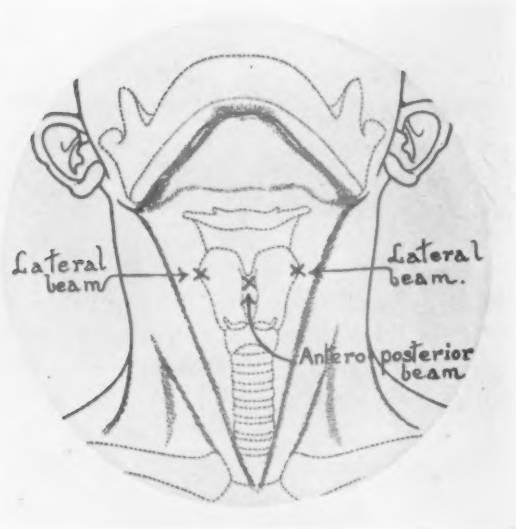


Fig. 15*c*. Case xii. Diagram showing the direction of the central beams of radiation.

daily. At the end of fifty-eight days 4,000 r per field had been given. Total dose 12,000 r.

Because of continued cigarette smoking, it was difficult to determine the exact time of beginning local mucous membrane reaction. (At no time during treatment or since have cigarettes been reduced below 20 per day.) It was definite, however, at the end of the third week, and a week later skin reaction was just noticeable with proper lighting.

At the end of a month (6,000 r total), there was definite growth regression and throat was symptomatically less irritable than at time of beginning treatment.

At the end of seven weeks there was no evidence of remaining growth, and at the end of another week (fifty-eight days) treatment was stopped (12,000 r total). At this time there was excessive secretion from the throat but at no time was there a generalized irritating semimembranous exudate. The skin was a dusky red but never weeping and there was no desquamation. There was no dryness, but during the second month, a transient period of reduced ability to taste food normally (smoking?). No edema at any time.

Six weeks later, the skin was normal, except for epilation, larynx normal to indirect and direct examination, no symptoms referable to throat, and voice normal. General appearance good, weight normal and blood count not reduced. During the entire treatment period he had played golf daily—9 to 27 holes per day, depending upon weather conditions.

He has remained entirely well in every way during the intervening year.

Comment. The case was operable by laryngectomy but, because of the infiltration, with a very narrow local margin. Generally, he was not a good surgical risk (alcohol, tobacco, transient high blood pressure).

Beyond that, the case is an example of the best I have been able to do so far by external irradiation. I am convinced, from numerous experiences, that the factors used in the three previous case examples would probably not have been adequate in this case.

The fact that only one year has elapsed is not the point. We have observed similar reactions for much longer. The case was selected because of its difficulties. The important point is the large amount of radiation we were able to give with very little by way of annoying symptoms at any time and with no gross damage to normal tissues at any time during treatment or since.

The improved quality of radiation, slow rate of delivery, and increased total quantity by reason of increasing both filter and distance are, all and each, factors of importance. Three fields give better distribution than two. We have tried an additional posterolateral beam from either side directed forward, but are not impressed with its value in either adaptability or physical efficiency.

The point may be raised that we stepped up filter, distance and time, and lowered r per minute, all together in this case. We have, however, tried changing each factor separately in other instances with sufficient frequency to be convinced of the *clinical* value of each altered step in spite of some physical calculations to the contrary.

With the treatment of all intensive roentgen therapy cases, I should like to emphasize the value of local and constitutional care as well.

At the time of daily examination, preceding the irradiation, the throat is carefully cleansed with alkaline pressure sprays, the nasal mucosa is shrunken slightly with ephedrine to improve and encourage nasal breathing, and the entire upper mucous membrane tract oiled finally with an oil spray.

A liver fraction is given parenterally, at the same time, to maintain or improve the blood level. Blood counts are carefully checked once or twice weekly, to govern the liver extract dosage and to indicate especially any drop in white cell count or alteration in the differential count.

The patient is instructed in warm alkaline throat irrigations at frequent and fixed intervals. A mild aromatic oil spray always follows the irrigation. Dietary matters are carefully supervised.

To many, this may seem an attempt to repeat what Coutard has said many times

before. Such is not the intent, although it is a pleasure to have the opportunity of adding my humble endorsement. We are deeply indebted for the basic principles which he has so ably laid down in therapeutic roentgen irradiation. His work has moved us ahead immeasurably in the treatment of laryngeal cancer.

However, if my interpretation be correct, he is interested in determining how far and by what technical means he can best and most completely control epithelial neoplastic growth with roentgen irradiation. My interest is in the strictly clinical problem of treating the laryngeal cancer patient, both locally and generally.

To this end, I am convinced that, today, our foremost aid is roentgen irradiation applied after the basic principles of Coutard. I am convinced that roentgen therapy in the "most enlightened manner" represents the backbone of treatment to be employed first in practically every case of true laryngeal cancer acceptable for treatment.

Beyond that, I am anxious to take advantage of all aids to treatment. It is not wise to depend upon one method alone and to the exclusion of others of proved value under certain conditions, even though they be limited. Reference is to the radium and surgical experience of the past.

Our method or combination of methods must be directed toward increasing the curability, restoration of function as fully as possible, and be acceptable both physically and aesthetically to the patient.

In my opinion, radium now occupies a more limited, yet much more definite and dignified position in the laryngeal cancer field. In certain of the advanced and more resistant types, and in some recurrent cases, with thyrotomy exposure, it affords a means of salvage not possible when roentgen irradiation is adhered to for too long. Constant observation of the case under roentgen irradiation will alone determine when to make a change.

A brief review of the surgical experience during the past century has been given. During the earlier years of surgical endeavor the results were even worse than with the earlier years of therapy by irradiation. Delavan stated that in 1900 he could find practically no reliable statistics. Obviously, this was due to the multiplicity of ever changing methods.

For the same reason, I regard irradiation statistics of doubtful value at present and question the advisability of submitting any. Five-year laryngeal irradiation statistics today are based on a technique usually obsolete at the time of publication and in such small numbers as to be misleading.

Since Delavan's surgical review in 1900, however, the methods have, by mass experience of the ablest laryngeal and some general surgeons, become standardized. There is such uniformity of opinion among those interested in the cure of laryngeal cancer by surgery that it would take a tremendous ego to attempt the introduction of new surgical measures at this time.

The data from standardized surgical techniques, and in a carefully selected material, are very impressive as far as they go. We must pay tribute to this work, developed before the period of effective radiation therapy.

Realizing the limitations and shortcomings of surgery per se for the cure and functional rehabilitation of the laryngeal cancer patient, it is now our responsibility to combine the advantages of radiation therapy with surgery where such combination offers more.

It is my opinion that the present status of radiation therapy renders total laryngectomy obsolete. The more conservative operation of thyrotomy for access, and at times for drainage, is extremely valuable, in conjunction with irradiation.

The early cancer is as favorable for irradiation as for surgical extirpation. The ultimate result is better. The real problem is the more advanced case in which surgery never has been interested.

In roentgen therapy I have referred to application in the "most enlightened manner." With me, at the moment, this refers

to the technical methods outlined in Case XII. These technical methods are constantly changing—for the better—based on added experience and the accumulation of accurate data from many sources.

At present the practical voltage for clinical work is 200 kv. It will remain so only until the experimental laboratories of research institutes and special units give us a more efficient range. Meanwhile, we have indeed very much to learn with 200 kv. in order that we may the more intelligently apply the radiation from a higher level, when that level has reasonably been determined upon.

The increase in both filter and distance has ample clinical endorsement, even though not entirely supported by physics. Where the increase should stop, or the relative ratio, is far from settled.

The size, shape and number of fields, the r per minute, r per day and manner of varying this, length and frequency of individual exposures, total exposure in terms of quantity, and optimum period for delivery of that quantity, are only a few of the problems to be worked out clinically and in conjunction with the physical, biophysical and histopathological laboratories, while we are waiting for more data on the voltage which we shall ultimately employ.

We must have this information if we are to utilize the higher voltages intelligently. We must have it if we are to continue extending the good work now well under way in increasing the curability and re-establishing perfect voice in the laryngeal cancer patient.

In conclusion, I wish to express my appreciation for the assistance and cooperation of my associate, Dr. James L. R. Young, in reviewing much clinical material and aiding with the illustrations for this lecture.

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A CASE OF EPIDERMOID (CHOLESTEATOMA) LYING UNDER THE SCALP AND OUTSIDE THE PERICRANIUM

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IN VIEW of the many papers that have appeared in the literature during the past seventeen years on the subject of epidermoid (cholesteatoma), it would seem that single case reports are no longer warranted. The case being reported, however, had its origin outside of the pericranium, a location that has not heretofore been described, although it is conceivable that some of the reported cases of intradiploic epidermoid may have had a similar origin that was obscured at the time of operation or autopsy.

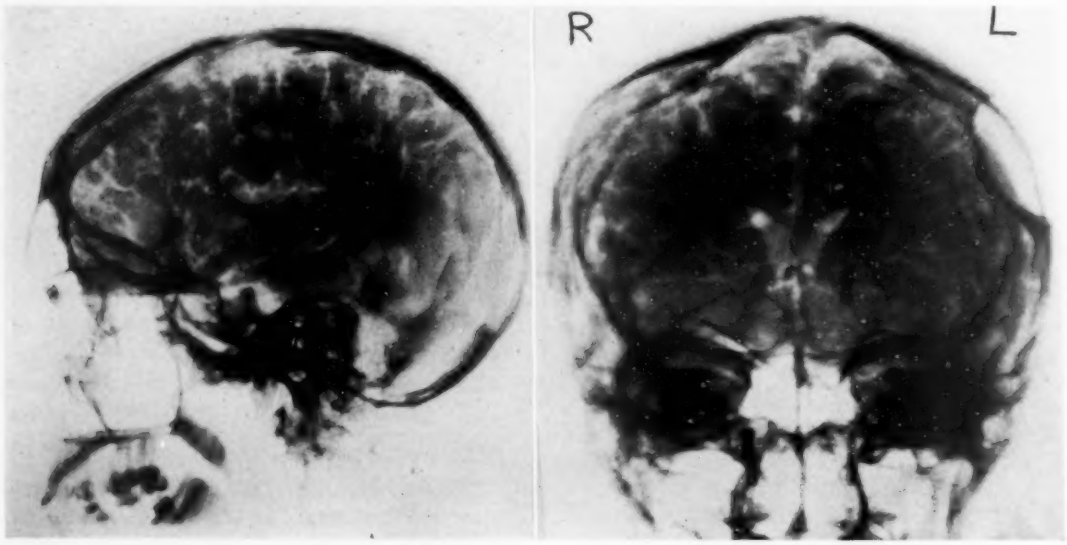

FIG. 1. Anteroposterior and lateral views of the skull after air had been injected. The extent of the deformity of the skull is shown, and the presence of air under it.

REPORT OF CASE

L. K., female, was referred to the University Hospital, Philadelphia, by Dr. Agnes Flack of Kingston, Pa. She was admitted to the Neurosurgical Service (No. 29504) on July 3, 1935. The findings at that time were characteristic of an intradiploic epidermoid. At operation it was found that the growth was completely outside of the pericranium. It was completely removed. Recovery was uneventful.

Six years prior to admission the patient noticed a hard rounded lump on the left side of her head. It was not fluctuant and caused her no pain until four months before admission when it started to increase in size and became troublesome when she combed her hair. She consulted her physician, who, thinking it was a sebaceous cyst, advised its removal. When the mass was incised at operation what was thought to be brain tissue appeared, and the surgeon felt a ridge of bone that made him think he was entering the cranial cavity. For this reason he closed the wound without doing anything further and had roentgenograms taken. They showed what appeared to be a defect in the cranial vault that measured about 4 cm. in diameter. She was then referred to the University Hospital for further treatment.

Examination. A young woman of twenty was seen who appeared to be in good health. There was a fluctuant mass on the left side of the head

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in the region of the frontotemporal suture 6 cm. from the midline. It measured 7.5 cm. in diameter. It did not pulsate. The center of this mass under the old incision was necrotic and very malodorous. There was a palpable lymph node behind the ear on the same side. The general physical examination was otherwise negative, as was the neurological examination. The white blood count was 11,200; the blood Wassermann was negative. Spinal puncture revealed a pressure of 120 mm. of water, 5 cells and a normal amount of protein.

Encephalography. Because the referring physician felt that there was an intracranial extension of the mass, an encephalogram was made on July 24. The films showed the ventricles to be well filled and of normal size. They were not deformed and the midline structures were not displaced. There was a moderate amount of air in the subarachnoid spaces of both sides, and air was present in the subarachnoid space under the defect as is seen in Figure 1. Because of this air in the subarachnoid space under the defect, it was felt that the growth did not have any intracranial extension, and operation was decided on.

Operation. August 9, 1935; Dr. Francis C. Grant. "The whole incision was reopened. A curette was passed about the capsule of the lesion and the mass, which was white and foul smelling, was removed. The capsule was white and in places flaky and seemed unbroken at any point. The cyst had hollowed out for itself a nest in the underlying bone to a depth of probably 1.5 cm. The bone was entirely intact and without defect. Furthermore, the bone was completely covered in all areas by intact periosteum. It was an extremely simple matter to shell out this cyst from the bony nest. The skin

Fig. 2. Photograph of the scar taken eighteen months after operation. The depth of the depression is interesting.

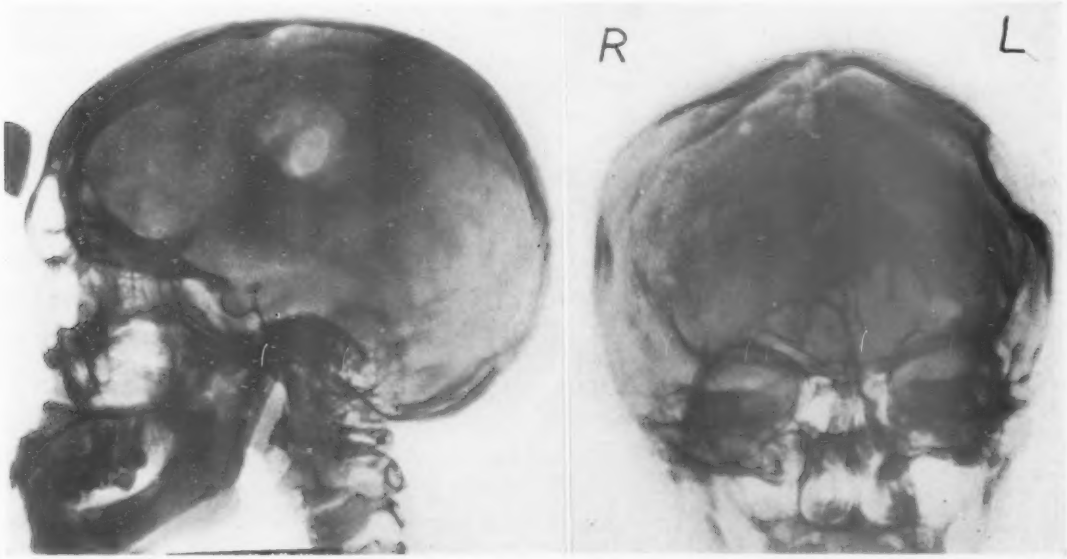

Fig. 3. Roentgenograms taken eighteen months after operation. Note the defect in the middle of the depressed area and the amount that the skull has pushed out toward its normal position.

FIG. 4. The gross specimen before it had been fixed.

flaps were allowed to fall into the cavity and were held in place by a moderate amount of packing."

Course. Her convalescence was uneventful and she was discharged on August 17, 1935, to her physician who was to continue dressing the granulating area. She was seen again in March, 1937. The wound was completely healed and formed a cup shaped depression (Fig. 2), the bottom of which was covered with thin epithelium that apparently contained no glandular elements. The ridge of bone was easily felt and is shown (Fig. 3) in the roentgenograms taken at that time. The films show that the original depression has partly filled in and that there is now a small defect in the center of this area that was not present at the time of the encephalogram. The erosion caused by the tumor had not apparently ceased at once following its removal. This defect could not be palpated through the overlying skin. As is seen in the photograph, the inner table of the skull has pushed out toward its normal position. She has no complaints and is working.

Pathological Report. The tumor was photographed immediately after operation (Fig. 4) and then placed in fixative in which it rapidly fell to pieces. The pathological reports were made on the basis of this disintegrated tumor, and the microscopic preparations were made under some difficulty. Gross description (Dr. B. J. Alpers): "The specimen consists of a disintegrated tumor. The outer portion is white, has the mother-of-pearl appearance, and the onion peel arrangement of a cholesteatoma. The inner portion of the tumor is disintegrated, but the fragments have a characteristic pearly sheen." Microscopic description (Dr. B. J. Alpers): "In a few places one sees what seems to be part of the capsule. This consists of a few layers of cells with round dark nuclei which are surrounded by dilated spaces. The cytoplasm is not clearly seen. The cells lie in a coarsely granular background" (Fig. 5, *A* and *B*). "These areas do not have the typical stratified appearance of cholesteatoma capsule, but they represent the closest appearance to capsule in the specimen. The rest of the tissue is composed of disintegrated cholesteatoma cells. Here and there one sees hard fibrils lying in parallel rows, constituting what is left of the stratum fibrosum" (Fig. 5, *C*).

BRIEF REVIEW OF THE RECENT LITERATURE

During the past seventeen years, starting with a paper by Bailey[1] in 1920, a great deal of material has appeared in the literature about the epidermoids of the central nervous system and its coverings. The pathology of these tumors was well described by Bailey in 1920 and supplemented by the pathological descriptions in his paper that appeared in 1924.[2] In this later paper he has differentiated between true "pearly tumors" that occur in the region of the middle ear, and which are rare, and the cholesteatomatous masses that so frequently occur as the result of long standing middle ear infection. Horrax,[3] writing in 1922, emphasized the relation of the epidermoids to the dermoids and described 3 examples of the hair-containing variety which he feels might as well be called hair-containing cholesteatomas, as one of them was not otherwise distinguishable from the true "pearly tumors" which do not contain it. He felt that these cases bear out the theory of Boström that these tumors are related as the epiblastic cells are, and that they differ only as the depth of the cells from which they originate differs. Critchley and Ferguson,[4] in 1928, reported on 9 cases that they had collected, and reviewed the status of the tumors up to that time. They felt that they should not be grouped with the dermoids in spite of their relationship to them.

Alpers and Harrow[5] reported on the intradiploic cholesteatomas in 1932, preferring that term to epidermoid. In 1935, Bucy[6] collected 13 cases of intradiploic tumors that had been reported as having 5 from Foerster's clinic that had not been reported. It is interesting to note that he separates them, according to their location, into diploic, 23 (his criteria for calling them diploic were not as strict as Bucy's);

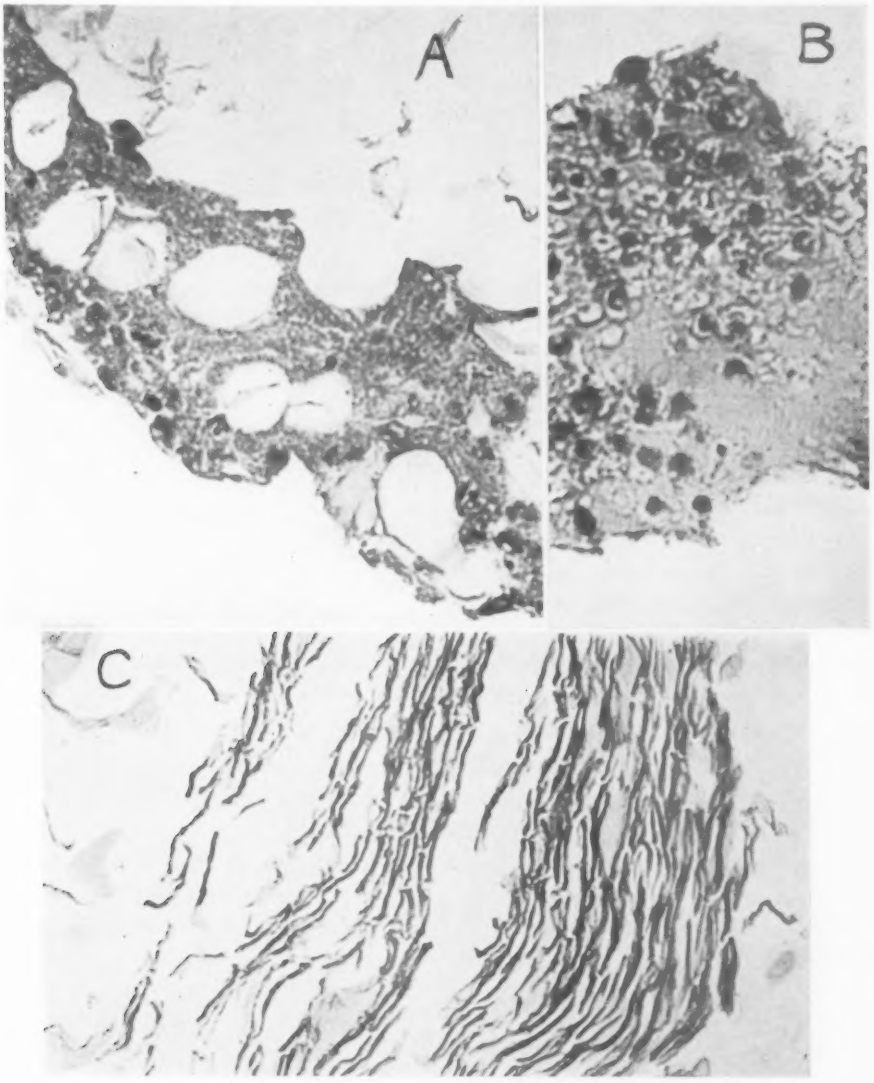

Fig. 5. Photomicrographs of the tumor. *A* and *B* show fragments of the capsule, and *C* shows an area of stratum fibrosum.

their apparent site of origin in the bones of the skull, and added 3 of his own. He described the characteristics of this group of epidermoids.

Mahoney,[7] in 1936, made an exhaustive review of the cases reported in the literature, collecting in all 142 cases, including arachnoidal (spinal), 7; fourth ventricle, 15; parapituitary, 44; and parapontine, 53. He found the greatest age incidence in the third, fourth, and fifth decades, being about the same for all of the groups, and commented on the fact that the dermoids occur at a younger age and the teratoids

at a still younger one. He goes into the theories of the origin of these tumors and falls in line with the now generally accepted theory that they are epidermoid. He feels that Kakeshita,[7] who is the most recent exponent of the endothelial theory of the origin of these tumors, is dealing with another type of neoplasm as shown by his photographs. He goes into a long discussion concerning the possible epithelial rests that may account for the sites of predilection of these growths.

COMMENT

The present case is out of the ordinary in that its site of origin was outside of the pericranium and that it had eroded the underlying bone by the effect of remote pressure. The roentgen findings were typical of the intradiploic epidermoids, which makes one wonder if more of these have not a similar origin. A visible defect in one of the tables of the skull appeared after the tumor was removed. If this had been present when the case was first seen, it is questionable whether the present localizing diagnosis could have been made. The pathological study of the tumor was difficult because of the degeneration that had taken place, but there can be no doubt that it is a typical epidermoid.

SUMMARY

A case of epidermoid is reported that had its site of origin outside of the pericranium under the scalp.

It is suggested that others of the so-called intradiploic epidermoids may well have had a similar origin that was obscured because of erosion of the underlying skull.

A brief review of the recent literature is given.

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EXCRETION OF FOREIGN SUBSTANCES BY THE LIVER AND THE QUESTION OF VISUALIZATION OF THE GALLBLADDER IN THE PRESENCE OF JAUNDICE*

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IT IS NOT always realized that the liver is a great excretory organ, comparable in many ways with the kidneys but excreting a different set of substances. It has been shown experimentally to be capable of excreting a very large number of foreign substances when introduced into the body.[1–12] Well over a hundred are known to be so excreted. There is a small list of substances excreted exclusively by the liver. The first of these to be thoroughly studied was phenoltetrachlorphthalein which was introduced for the purpose of liver function tests by Abel and Rowntree[13,14] in 1909. A large group of closely related substances, mostly dyes, was then found to be excreted largely or entirely by the liver. One of these, bromsulphthalein, introduced by Rosenthal and White[15] is an improvement on tetrachlorphenophthalein. Two others chemically related, also dyes, namely, rose bengal and azo rubin-S, are also excreted almost exclusively by the liver and are in use for liver function testing. There is a large list of other substances, such as congo-red, neutral red and many other dyes that are known to be excreted in large part or in some instances exclusively by the liver but these have not come into such general use.

It should be mentioned that in the case of many substances which are excreted by both liver and kidneys, the extent to which they are excreted by the one depends on the function of the other. Thus, with substances that are excreted almost entirely under normal conditions by the liver, if the liver is badly damaged or is excluded from the circulation experimentally, the substance is excreted by the kidneys.

In their great pioneering work, which led to the introduction of cholecystography, Graham and Cole tested out over forty iodine or bromine derivatives of these substances known to be excreted partially or wholly by the liver.[16] They found thirteen of them, all of them phthalein derivatives, to be capable of producing cholecystograms when combined with the heavy atom halogens, iodine or bromine. For various practical reasons two of them, phenoltetraiodophthalein, which is now used exclusively for intravenous cholecystography, and tetraiodophenolphthalein, which is the choice for oral cholecystography, were found to be the best.

What determines whether a substance is excreted by the liver or by the kidneys? There are a number of factors which play a rôle. Foreign substances of a colloidal nature or such as can only be obtained in colloidal solution, and foreign substances which are soluble only in fat or in fat solvents tend to be excreted by the liver rather than by the kidneys,[17] while easily soluble crystalloids are more frequently excreted by the kidneys. Solubility in alkaline or acid reactions also plays a large part. Substances that are only soluble in alkaline solutions or as alkaline salts are usually excreted by the liver. (This is true of the substances used in visualizing the gallbladder.) In the case of some chemicals, excretion by the liver or kidneys respectively depends on a chemical transformation, usually a coupling with some other substance.

The reason why so great a number of the substances whose excretion by the liver has been studied have been dyes is simply that

* Read at the Eastern Conference of Radiologists, New York, Jan. 29–30, 1937.

the excretion of a dye offers itself so readily for experimental study. But there is every reason to believe that a very large number of chemical compounds which have not the property of intense color will be found also to be excreted by the liver when suitable studies are made. I wish to emphasize that, marvelous as the progress has been since the introduction of cholecystography, the field should not be regarded as a closed one. It seems almost certain that prolonged and systematic work will reveal that there are other compounds which can be used, some of which may be even more advantageous than those which we now have for cholecystography. The field, however, is a difficult one and rapid progress cannot be expected.

My own experimental work in the field of substances excreted by the liver has been in the direction of searching for a biliary antiseptic,[18] and, just as Graham and Cole had to disregard a very large number of compounds which they tried for visualization because of their toxicity, I had to disregard many bactericidal substances which were excreted exclusively or in very large part by the liver because of their toxic effects. Extreme purity of the preparation is of great importance in experimenting in this field, and it is possible that some of the drugs that were rejected because of their toxicity might have been acceptable if purer products had been at hand. This is illustrated, for example, by the early work of Graham and Cole when tetraiodophenolphthalein, which was later found to be most useful, was rejected in favor of the brom compound because of the supposed toxicity of the former.

With regard to the toxicity of the tetraiodo compounds now in use for gallbladder visualization, they have, on the whole, turned out to be surprisingly innocuous. I am myself perhaps partially responsible for spreading the fear of the toxicity of these drugs because in 1925, together with Abramson, I published[19] some experiments in which it was shown that a dose about five times that used for cholecystography was capable of producing necrosis of liver cells when given intravenously. I therefore warned that it might be dangerous to use this dye in the presence of liver disease. In the early years of cholecystography rather frequent and severe reactions which were obtained on intravenous use of the dyes seemed to confirm the idea that they were somewhat dangerous. However, further clinical experience has shown that many of the earlier reactions were due to impure preparations or faulty technique and, in spite of the thousands of cases in which these dyes have been used, there is, so far as I am aware, only one death which has been directly attributed to them, and there is no evidence that they ever produce clinical liver damage.

For this reason, in recent years a number of workers have had the courage to disregard the earlier warning against attempts to visualize the gallbladder in the presence of jaundice. In 1930, Rudisill[20] published the results of intravenous visualization in which he used the full dose, 3.5 grams, of tetraiodophenolphthalein intravenously in 10 cases with no untoward effects. Eight of these were cases of catarrhal jaundice and in 7 of these the gallbladder was visualized. One case was deeply jaundiced due to stone in the common duct; and a gallbladder full of stones was well visualized. In 1933, Foley[21] collected 29 cases at the Cook County Hospital in which visualization was attempted either by the oral or intravenous method. Of these, 16 were medical jaundice, and in 11 of them the gallbladder was visualized—all but one by the oral route. Thirteen were surgical jaundice, that is obstruction due to carcinoma or stone, and none of these visualized. Jacobi,[22] in 1936, also attempted gallbladder visualization in toxic hepatitis and was successful in 7 out of 8 cases.

The latest work is that of Foote and Carr.[23] They use a very cautious intravenous method giving fractional doses of the dye to a total of 0.75 gram, by slow drip well diluted in 1,000 cc. of 10 per cent glucose solution on three successive days.

It is extremely important during the time of these injections that the patient should be on a strictly fat-free diet. Foote and Carr found that in a considerable proportion of the cases of hepatitis the gallbladder would be visualized about twenty hours after the last injection and would empty normally after a fat meal. In a small number of cases of obstructive jaundice the gallbladder could also be visualized at between twenty and forty-eight hours, but failed to empty after a fat meal and the dye only gradually disappeared by absorption, presumably through the gallbladder wall.

From all this work it seems clear that, provided one uses good judgment in selecting cases of jaundice in which the liver function tests do not indicate grave damage to the liver parenchyma, one is justified in attempting gallbladder visualization either by the oral or the intravenous route in spite of the presence of jaundice. Successful visualization, followed by normal emptying, points strongly to hepatitis as the cause of the jaundice. Successful filling with failure to empty after the fat meal points to obstructive jaundice. However, failure of the gallbladder to visualize in the presence of jaundice cannot be used in diagnosis at all, because it might equally well be due to gallbladder disease or to the failure of the liver parenchyma to excrete the dye. In our own experience we have tried the Foote-Carr method so far only six times and have not yet secured a good visualization. We have a feeling that the dosage is perhaps a little overcautious and intend in the future to experiment carefully with increasing it.

With regard to the liver function tests which are of use in deciding whether it is safe to attempt cholecystography in the presence of jaundice, the depth of the jaundice (and correspondingly the amount of bilirubin in the blood plasma) is not a point of great importance, although it is true that in a general way cases with a very profound jaundice are more likely to have a damaged liver function. However, a successful gallbladder visualization has been reported in cases with icterus index as high as 100 (Meulengracht) and unless the icterus index is extremely high, say over 100, it should not be a contraindication. A guide of great value to the extent of liver damage is the percentage of cholesterol esters in the blood. Normally these should be 100 or more milligrams per 100 cc. If they are 40 mg. or less they indicate severe damage to the liver and it is probably unwise to risk an attempt at gallbladder visualization.

A functional test of great value is the galactose tolerance test. The excretion of 3 or more grams of galactose in this test points definitely to parenchymal liver damage and suggests caution in the use of the dye. However, as the majority of cases of hepatitis do give an increased galactose excretion this should not in itself be regarded as an absolute contraindication but should be taken into consideration along with the other function tests.

Exactly the same thing may be said of Quick's hippuric acid synthesis test except that in this instance it is the finding of less than 3 grams of hippuric acid in the urine which points definitely to liver damage. The mode of application of this finding is exactly the same as the galactose test. The two tests may be regarded as of equal value and a positive result with either test is sufficient to point to liver damage.

The finding of tyrosin in the urine by the method of Lichtman and Sobotka may be regarded as a contraindication to the use of dye, since, as a rule, it is only found in cases of more severe hepatitis.

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PHYSIOLOGIC PRINCIPLES IN ROENTGENOGRAPHIC VISUALIZATION OF THE BILIARY TRACT AFTER THE INJECTION OF LIPIODOL*

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RECENT advances in the physiology of the biliary tract may be applied to lipiodol visualization following choledochal intubation.

The biliary ducts have their origin between the rows of liver cells which line the fine bile canaliculi, and lead through the canal of Hering into the beginning of true bile ducts. The maximum secretory pressure of the liver is about 350 mm. of water; above that point the liver stops secreting.[1] The normal resistance of the sphincter of Oddi averages 150 mm. of water.[2] The liver bile therefore enters the gallbladder. The gallbladder, both by its ability to dilate and also to concentrate the bile, acts as a storehouse and keeps the intraductal pressure at about 100 mm. of water.[3] Acid or fat entering the duodenum stimulates the formation of cholecystokinin in the duodenal mucosa.[4] This hormone circulating through the blood causes active contraction of the gallbladder, forcing the bile through the sphincter of Oddi. The maximum force of contraction which the gallbladder can exert is about 250 mm. of water.[5] The result is that although the sphincter of Oddi can be forced open by active contraction of the gallbladder, bile cannot ordinarily be forced up the hepatic ducts against the higher secretory pressure of the liver. Similarly after T-tube intubation, injection of lipiodol will normally outline the choledochus only. The hepatic ducts will not be visualized since the sphincter of Oddi will give way before lipiodol can be forced up the hepatic ducts.

We found that the presence or absence of sphincter of Oddi spasm caused changes in the appearance of the biliary tract after lipiodol visualization. The manometric resistance of the sphincter of Oddi was recorded directly on a kymogram,[2] and these readings were correlated with the findings after lipiodol injection.

FIG. 1. Lipiodol visualizes the choledochus and the termination of the hepatic ducts only, and enters the duodenum readily. This is indicative of a normal resistance of the sphincter of Oddi, and is confirmed by finding the manometric resistance to be 140 mm. of water.

Ordinarily, when lipiodol is injected it passes directly into the duodenum, only the common bile duct and the distal ends of the hepatic ducts being visualized. Thus, in a patient in whom the resistance of the sphincter was 140 mm. of water, the lipiodol could be seen entering the duodenum without visualization of the hepatic duct (Fig. 1). In another patient, by actual

* From the Surgical Service of Dr. Ralph Colp, the Mount Sinai Hospital, New York. Read at the Eastern Conference of Radiologists, New York, Jan. 29–30, 1937.
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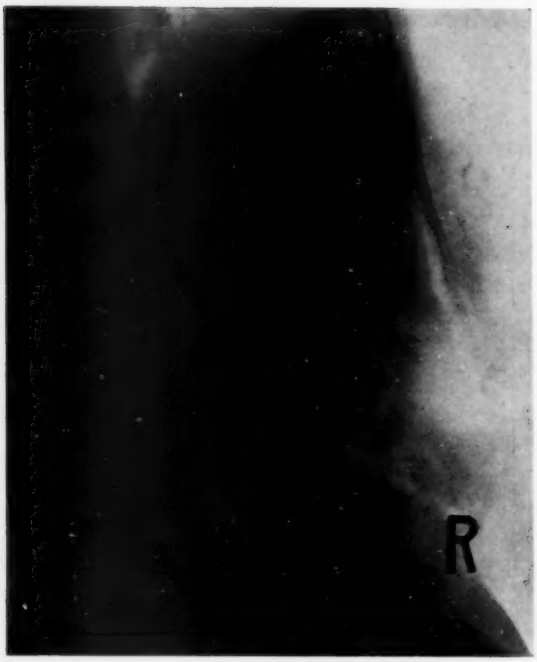

Fig. 2. Lipiodol injection nine days after operation shows that sufficient pressure had to be used to outline the hepatic ducts rather fully before a few drops of lipiodol entered the duodenum. The manometric resistance was found to be 190–220 mm. of water. Note that the ampulla of Vater is distended with lipiodol. The intramural portion of the choledochus is not visualized due to pressure of the duodenal wall.

Fig. 3. Same case as in Figure 2. Visualization on the twelfth day after operation. The hepatic ducts are outlined in some detail before lipiodol is seen entering the duodenum (lateral view). The manometric resistance of the sphincter of Oddi was 220–260 mm. of water at that time.

manometric measurements, the resistance of the sphincter was found to be 190–220 mm. of water nine days after operation. Roentgen visualization at that time (Fig. 2) showed the hepatic ducts to be outlined fairly high up, while the ampulla of Vater could be seen distended by the lipiodol. A clear space above the ampulla resulted from the pressure of the duodenal wall on the intramural portion of the duct. Three days later (Fig. 3) another roentgen examination after the injection of lipiodol again outlined the hepatic ducts before lipiodol could be forced into the duodenum. The actual manometric resistance at that time was found to be 220–260 mm. of water. In a third case (Fig. 4) examination was made eleven days after operation. As can be seen, the hepatic ducts were outlined to a considerable extent before lipiodol could be forced into the duodenum through a fine narrow channel. The resistance of the sphincter was found to be 220

Fig. 4. The hepatic ducts are extensively outlined before lipiodol is seen entering the duodenum through a long fine channel. The manometric resistance in this patient was 220 mm. of water.

mm. of water. The presence of spasm was further supported by the finding of pancreatic enzymes in the biliary drainage. In short, if lipiodol enters the duodenum without visualization of the hepatics, the sphincter tone is normal or low. If the hepatic ducts are visualized before lipiodol can be forced into the duodenum, the sphincter is spastic.

A kymographic apparatus previously described[2] was used to investigate the action of drugs which were reported to cause functional spasm of the sphincter of Oddi. It was found that morphine caused very severe and prolonged spasm of the sphincter of Oddi. This pharmacologic action was utilized to visualize the biliary duct system after choledochal intubation. The following technique was used: Under roentgenoscopic control, lipiodol was injected by means of a 50 cc. syringe until it was seen to enter the duodenum. A roentgenogram was then taken. Ten minutes was then allowed so that the duodenum would become clear of lipiodol. Morphine (gr. $\frac{1}{4}$) was then administered hypodermically, and five minutes later lipiodol was again injected very slowly under roentgenoscopic control. At this time the entire biliary tree could be visualized. Anteroposterior and lateral roentgenograms were taken.

Fig. 5. In this case the choledochus is outlined very poorly, the lipiodol entering the duodenum promptly. The manometric resistance here was 130 mm. of water.

Fig. 6. Lipiodol injected five minutes after the administration of $\frac{1}{4}$ gr. of morphine, and fifteen minutes after taking Figure 5. Due to spasm of the sphincter of Oddi, the whole biliary tract could be clearly outlined.

Roentgen examination of a patient, in whom the sphincter of Oddi resistance was 130 mm. of water, showed the lipiodol entering the duodenum with ease (Fig. 5). The common duct and the terminal hepatic ducts were outlined in a sketchy manner. Lipiodol injection five minutes after morphine administration (Fig. 6) outlined the whole biliary tract, while no lipiodol could be seen in the duodenum. Occasionally where the anatomic relations are such that the pancreatic duct enters the choledochus above the sphincter of Oddi, the pancreatic ducts may be outlined in part or wholly.

Our experience indicates that implantation of a T-tube is necessary for good roentgen visualization of the biliary tract postoperatively. A straight tube is not

satisfactory because it is very apt to be dislodged easily. Roentgen examination with lipiodol should not be attempted before the T-tube is firmly surrounded by the healing tissues of the biliary sinus, i.e., about the twelfth day after operation. Attempted visualization before the tube is firmly implanted results in the regurgitation of the lipiodol around the tube. No pressure can then be exerted to force open a spastic sphincter; as a result functional spasm cannot be differentiated from organic obstruction. If the sphincter is atonic, the lipiodol enters the duodenum easily and the ducts cannot be clearly outlined. A tube size 18-22F. is preferred. A smaller one is apt to become blocked, while a larger one prevents the tissues from healing firmly around it.

CONCLUSIONS

When the T-tube fits firmly in the sinus, visualization of the biliary tract with lipiodol yields the following valuable information: (1) the presence or absence of organic biliary obstruction; (2) the presence or absence of spasm of the sphincter of Oddi; (3) the outline of the whole biliary tract by the use of morphine, to determine the presence of calculi or of cancer.

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EMPTYING OF THE NORMAL GALLBLADDER*

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THE following presentation is intended as a review of the physiology of normal gallbladder emptying, together with a preliminary report on some pertinent experiments that have been performed in this Department.

GALLBLADDER CONTRACTION

In spite of much serious opposition in the past, there is very little doubt today that the gallbladder empties by tonic contraction of its wall and that the bile is evacuated through the cystic duct. There appear to be two types of motor activity: (1) a tonic contraction which produces a sustained rise in pressure persisting from five to thirty minutes or more; (2) a tonus rhythm with rhythmic contraction and relaxation, there being two to six waves per minute. In each type the muscular coat of the gallbladder may contract as a whole or in irregular segments. The tonic contraction is normally followed by opening of the sphincter of Oddi. The pressure which the contraction produces is considerable but is less than the secretory pressure of the liver.

The most efficient substances producing gallbladder contraction are the fats, lethicin, fatty and mineral acids when introduced into the duodenum or upper part of the intestine. Ivy[7] believes that the fatty substances cause the production of a hormone, cholecystokinin, which in turn produces gallbladder contraction. The efficiency of cream, egg yolk, olive oil, etc., depends on the concentration of these substances in the duodenum and on the concentration of cholecystokinin produced. The exact mechanism involved in its action is not well established but apparently it produces a sustained tonic contraction of the muscle; nervous mechanisms, however, are said also to play a part. Psychogenic emptying of the gallbladder does not occur. Vomiting has no effect nor would it be anticipated because the increase in intra-abdominal pressure is the same over the duodenum as it is over the gallbladder. A flushing action by hepatic bile is described by Graham and his coworkers,[6] but according to Ivy it is not an essential part of the process, if it occurs at all. On the other hand, Doubilet and Colp,[3] to explain the passage of bile after duodenal administration of magnesium sulphate, suggest that the rapid evacuation of hepatic bile through the relaxed sphincter sucks the gallbladder bile along with it by negative pressure.

RELATION OF GALLBLADDER CONTRACTION AND THE SPHINCTER OF ODDI

There is said to be a reciprocal relationship between gallbladder emptying and relaxation of the sphincter of Oddi which has been assumed to be nervous (Potter and Mann, Birch and Boyden)[7] but the details of the mechanism are admittedly unknown. It is probable, however, that in addition to or exclusive of any nervous mechanism, control of the sphincter is humoral. In the studies of Sandblom, Voegtlin and Ivy[8] on the effect of cholecystokinin on the sphincter of Oddi, an initial increase in resistance to the flow of bile from common duct to duodenum was found, followed by a decrease. These changes were correlated with a periodic increase and decrease in the motility and tone of the duodenum. The effects were independent of the gallbladder since they would occur after cholecystectomy. These authors suggest that the hormone primarily decreases the intramural resistance but increases the duodenal tone and the latter temporarily increases the common duct pressure.

* From the Mount Sinai Hospital, Service of Dr. Leopold Jaches. Read at the Eastern Conference of Radiologists, New York, Jan. 29–30, 1937.

Fig. 1. Gallbladder partly emptied after the administration of three egg yolks. Arrows point to common duct.

EMPTYING AFTER A FAT MEAL

Evacuation of the gallbladder after a fat meal is said to occur in several phases. The viscus usually contracts to 50 or 25 per cent of its size within thirty minutes. Then, there is a period of quiescence for about an hour followed by a second contraction, there being further similar cycles until evacuation is complete. The first contraction phase is undoubtedly of most significance from the functional point of view and is the phase in which the biliary tracts may be visualized.

There have been large numbers of reports on the normal emptying time of the gallbladder. With the aid of Dr. Frederick Rosenthal, the Graham tests made in this Department have been reviewed and 170 representative cases which visualized normally without any evidence of stone were analyzed more carefully. These patients were told to take a regular lunch and, in addition, an eggnog (one raw egg and a glass of milk) an hour and a half before returning to the Department. Of these, only 23 cases showed residues of 50 per cent or more. Many of them initially showed large gallbladder shadows and we gained the impression that when the gallbladder shadow was initially large there was not apt to be complete emptying, and that this was a normal finding.

The clinical histories of these 23 cases were further studied to determine whether an abnormality in gallbladder function was definitely suggested. In only 5 could a diagnosis of chronic cholecystitis still be considered in the face of the finding of normal visualization, and unfortunately these particular cases were not subjected to surgical exploration. Dr. Colp's data,[2] however, suggest that the most common discrepancy between the roentgen finding of a normally visualized gallbladder and the operative finding of disease was in the demonstration of single or multiple small stones at operation, not shown roentgenologically. Review of the Graham tests in these 3 cases showed no delay in emptying.

Two cases in the group were found to have obstructing peptic ulcers. This emphasized the need for excluding an organic or functional obstruction to the passage of the fat meal as a possible cause for delayed emptying. It is probably the most important factor accounting for the variations in gallbladder emptying time reported in the literature. The type of fat meal is probably of secondary importance.

The evidence from this review indicated that, with pyloric obstruction excluded, the gallbladder should empty more than 50 per cent within an hour after a fat meal but that slower emptying was not necessarily abnormal. A second fat meal given at the end of this hour often produced rapid and adequate emptying.

GALLBLADDER EMPTYING ON FAT-FREE DIETS

It has been known that in fasting or with the administration of carbohydrate diets, the gallbladder shadow may persist for twenty-four hours or longer. The problem is complicated since normally tetraiodo-

phenolphthalein is slowly absorbed by the gallbladder mucosa. Copher[7] reported in 1925 that a persistent gallbladder shadow may be maintained by the daily injection of tetraiodophenolphthalein. To obtain further information on this subject, 11 patients were placed on a fat-free diet consisting of approximately 1,450 calories per day with 325 grams of carbohydrate, 29 grams of protein and no fat. Only ward cases with no clinical evidence of gallbladder disease, and whose diets could be accurately controlled, were chosen for study. Five cases were given 5 grams of tetraiodophenolphthalein by mouth at 12 noon and a second 5 grams at 7 P.M., the patient having been placed on the carbohydrate diet the day before. Six cases were given the same total dose of dye but over a period of forty-eight hours.

The results were not entirely uniform but the evidence seemed to indicate that in most cases when a patient is placed on a carbohydrate diet the size of the gallbladder remains constant for at least five days and that its density diminishes due to absorption of dye by the gallbladder mucosa. The lack of uniformity of the results is difficult to explain. Dr. Doubilet suggested to me that since mineral acid produces emptying of the gallbladder even in the absence of a fat meal there might perhaps be some relation between rapidity of emptying and gastric acidity. Although our data are incomplete, we have some evidence to suggest such a relationship since hyperchlorhydria has been found to be associated with a more rapid disappearance of the gallbladder shadow in some cases. Further work is in progress concerning this point. It might perhaps be of significance in the poor visualization sometimes found with duodenal ulcer.

The results in these 11 cases may have other than academic interest also in relation to the use of fat-free diets in cholelithiasis and cholecystitis. There is reason to believe that stasis is an important factor in the formation of biliary calculi. The present results indicate that fat-free diets

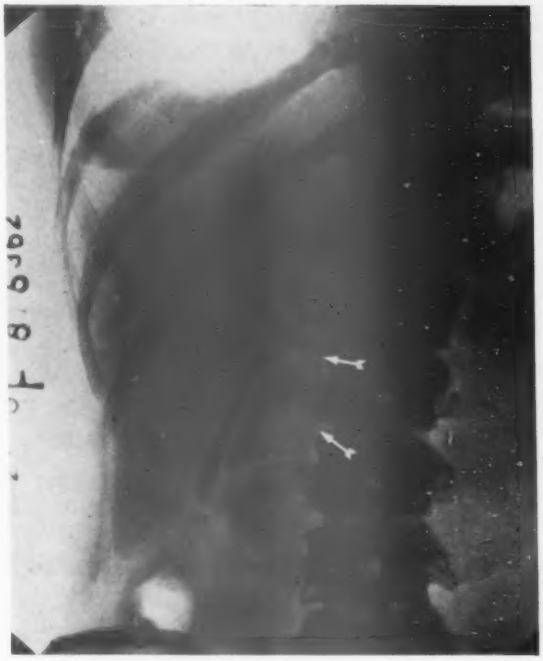

FIG. 2. Gallbladder almost completely emptied fifteen minutes after the administration of three egg yolks by mouth. The cystic duct is tortuous. Arrows point to common duct.

are certainly associated with gallbladder bile stasis and give further data to justify the administration of eggs and cream as is advocated, for example, by Brown and Dolkart.[1]

It has been stated in the literature[4] that as bile enters the gallbladder the hepatic bile is layered on the concentrated bile already present and, in turn, is concentrated. This is said to be shown by the demonstration of levels in the erect position when the Graham test is followed through for several days. We were not able to confirm these observations. Examinations were made each day on the 11 cases under discussion and no levels were shown. It would seem more likely that the mottling of the gallbladder shadow which was interpreted as being due to the presence of levels was due to the separation of dye in the stagnant bile as Foote and Carr[5] have suggested.

BILIARY DUCT VISUALIZATION

Emptying of the normal gallbladder can be obtained regularly when fat is intro-

duced into the duodenum by duodenal tube. This usually occurs within five to ten minutes. It has been stated in the past[7] that in about 30 per cent of cases given a fat meal by mouth the gallbladder is seen to have contracted and the cystic duct, with or without the common duct, is visualized. It is our experience that if a high concentration of fat is obtained in the duodenum so that a high concentration of cholecystokinin is obtained, the cystic and common ducts can be visualized regularly. Dr. Woodruff and I have examined a series of cases by the following technique: The gallbladder was visualized in the usual way. A fatty meal consisting of three egg yolks in a small amount of milk was given. Roentgen examinations were made ten, twenty and thirty minutes later. In at least 75 per cent of the cases in which emptying took place at all, the ducts were visualized. Such a method of study is of greater importance than the exclusive determination of the ability of the gallbladder to empty within a certain period of time. The demonstration of a normal cystic and common duct provides a valuable confirmation of a normal function of the gallbladder and of the sphincter of Oddi.

The ducts often remain visualized for fifteen to twenty minutes, indicating that gallbladder evacuation takes place through a prolonged contraction of the muscle and that the primary increased resistance at the sphincter due to cholecystokinin probably lasts for at least this length of time before relaxation occurs.

EFFECTS OF DRUGS

There is considerable evidence to suggest that morphine administration results in sphincter spasm. Theoretically, then, it should be possible to demonstrate the common duct more often by initiating gallbladder emptying with egg yolk and following by morphine. A series of experiments were performed therefore along these lines. Three egg yolks were given by mouth followed in ten minutes by morphine gr. 1/6 hypodermically. There was marked delay in gallbladder emptying, the viscus being unchanged in size four hours later; the ducts were not visualized. A possible explanation here was that the morphine produced sufficient pylorospasm to interfere with the passage of the egg yolk into the duodenum. For this reason, in another group of experiments morphine was given half an hour after the egg yolk when, judging by our previous experience, emptying would have begun. Twenty-four hours later, the gallbladder had not changed materially in size: in some cases, the shadow seemed even larger. Yet egg yolk given on this second day produced normal emptying within half an hour and normal visualization of the ducts. A more crucial experiment was then performed. Egg yolk was given and the gallbladder shadow watched roentgenoscopically until it became distinctly smaller. On the roentgenograms the cystic duct showed distinctly. Morphine was then given hypodermically and within ten minutes the duct was no longer visible. Gallbladder emptying was completely inhibited, its shadow being unchanged in size four hours later. These experiments indicate that, in the human, morphine interferes seriously with gallbladder evacuation following a fat meal. The factor of pylorospasm is important but there is no doubt that morphine has a direct effect.

Any action that morphine has on the gallbladder musculature should increase contraction. Experimental data suggest that in dogs and rabbits the amplitude of the tonus rhythm is augmented and we know that in general morphine produces spasm of smooth muscle. It would seem most likely, then, that morphine produces sphincteric spasm perhaps through increased duodenal tone and there is a rise in common duct pressure. The gallbladder cannot empty because the pressure produced in the gallbladder by contraction does not exceed the pressure in the duct. It may even become larger due to continued secretion of the liver.

Many workers have indicated that nitroglycerin produces relaxation of the

sphincter. After gallbladder visualization in the usual manner, egg yolks were given by mouth to produce contraction. Nitroglycerin gr. 1/100 placed under the tongue produced inhibition of emptying promptly but temporarily, since two hours later normal contraction occurred with visualization of the ducts. Presumably, here, the nitroglycerin also produced relaxation of the gallbladder musculature which overcame the effect of the cholecystokinin. Since the nitroglycerin effect was transient, emptying proceeded normally, when its effect had worn off.

The presence of sphincteric action of the neck of the gallbladder has been suggested. Although there is little doubt that the valves of Heister could contract down and produce a very small lumen there is no actual proof that a definite sphincter is present. Nor is it necessary to assume its existence in order to explain the observed facts. It seems more likely that repeated failure to empty after a fat meal with nonvisualization of the ducts might rather be due to a cystic duct calculus.

SUMMARY

1. The normal gallbladder in fasting individuals or in those on a carbohydrate diet does not contract for at least five days and probably stays filled much longer. The tetraiodophenolphthalein is absorbed by the gallbladder mucosa.

2. Gallbladder evacuation depends on the production of cholecystokinin, which, in turn, depends upon the introduction of fats or acids into the duodenum in fairly high concentration.

3. The normal gallbladder usually empties to less than half its size within thirty minutes after the administration of three egg yolks, and the cystic duct, and also often the common duct, can be demonstrated. This provides a valuable confirmation of normal function.

4. Function cannot be considered abnormal when there is delayed emptying. A second egg yolk meal should be given. Pylorospasm or pyloric obstruction must be excluded as possible causes.

5. The biliary ducts often remain visualized for fifteen to twenty minutes due to the primary action of cholecystokinin, namely, contraction of the gallbladder and increased intramural resistance at the sphincter of Oddi.

6. Morphine completely prevents evacuation of the normal gallbladder after a fat meal. This is apparently due to spasm of the sphincter of Oddi and not to a relaxation of the gallbladder musculature: pylorospasm is also an indirect factor. Visualization of the biliary ducts is therefore not obtained. Nitroglycerin also produces a definite but temporary inhibition of gallbladder emptying.

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CHOLECYSTOGRAPHY AND ITS CORRELATION WITH GALLBLADDER PATHOLOGY*

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IN 1925, Graham, Cole and Copher,[2] described a method by which, following the injection of tetraiodo- or tetrabromphenolphthalein, a normal gallbladder could be visualized, and if abnormalities were present in that viscus, they would be evident by certain roentgenological findings. They stated that the failure to obtain any shadow invariably indicated definite pathology of the biliary tract, although it was conceivable in instances of a very serious disturbance of hepatic function that an insufficient amount of the substance might be secreted to produce a shadow even without any appreciable alteration of the gallbladder. Abnormalities of lesser degree have shown themselves by such phenomena as the late appearance of a shadow, failure of shadow, failure to diminish in size, distortion of outline, irregular mottling, and negative shadows occasioned by the presence of calculi. They felt that cholecystography was an index of function of the gallbladder, rather than one which showed sharply distinct pathological lesions, and that the sensitiveness of cholecystography in revealing abnormalities of function of the gallbladder was one of the most striking assets in the diagnosis of slight degree of cholecystitis.

While the diagnosis of gallbladder disease may usually be made from the history in the majority of cases, other diseases may simulate it so closely that it may be extremely difficult in some instances to arrive at a proper differential diagnosis. It is essentially true that the presence of a cholecystitis of a mild degree, with or without stone, may often cause a clinical picture of obscure symptomatology. Cholecystography has been of great importance, not only from a confirmatory standpoint, but in the diagnosis of the more obscure cases of frank gallbladder disease. It has, in addition, proved to be an effective means of assaying the functional impairment of the gallbladder in the early phases of cholecystitis.

The study of oral cholecystography, checked by the observations obtained by surgical exploration, was undertaken not only to determine the reliability of the method, but also to ascertain whether certain roentgen findings could be interpreted as indicative of definite pathological states.

These cases, 208 in number, are grouped according to the findings revealed by cholecystography, and the following classifications have been arbitrarily made.

1. Cases in which the cholecystogram was reported as normal and in which operation revealed a pathological gallbladder.
2. Cases in which there were normal filling and emptying of the gallbladder, and in which radiopaque and radiotranslucent shadows were present.
3. Cases in which there was poor visualization of the gallbladder without stone.
4. Cases in which there was poor visualization of the gallbladder, and in which radiopaque and radiotranslucent shadows were present.
5. Cases in which there was no visualization of the gallbladder without stone.
6. Cases in which there was no visualization of the gallbladder and in which stones were present.

1. *Cases in Which the Cholecystogram Was Reported as Normal and in Which Operation Revealed a Pathological Viscus.* There were 5 cases in which the cholecystograms were reported normal, and in which operation disclosed definite pathology of the gallbladder.

* From the Department of Roentgenology and the Surgical Services of the Mount Sinai Hospital, New York. Read at the Eastern Conference of Radiologists, New York, Jan. 29–30, 1937.

Case I (No. 322957). G. K., a female, aged twenty-five, was admitted February 9, 1931, and discharged February 23, 1931.

Following a pregnancy twenty months ago, she experienced recurrent attacks of biliary colic, which were never associated with jaundice or fever.

Because of some slight costovertebral tenderness, cystoscopic investigation was done and revealed no abnormality. Examination of the gallbladder after the oral administration of dye showed that the viscus was visualized and was normal in size, filling and emptying. Considerable deformity in shape suggested the presence of adhesions.

Operation disclosed a chronically inflamed, thickened gallbladder with a single small stone in the neck. The gallbladder was found adherent to the duodenum.

Following cholecystectomy, the patient made an uneventful recovery and was discharged on the fourteenth postoperative day.

The pathological report showed a chronic cholecystitis.

Case II (No. 317150). F. C., a female, aged thirty-four, was admitted on August 31, 1934, and discharged on September 15, 1934.

She gave a two-year history of frequent severe attacks of epigastric and right upper quadrant pain. One year ago she had an attack associated with jaundice.

Examination of the gallbladder, after oral administration of dye, showed this viscus to be normal in size, shape, filling and emptying time.

Operation disclosed the gallbladder to be moderately dilated and its walls definitely thickened. There were no stones. The cystic duct was narrowed, but patent.

The pathological report disclosed chronic cholecystitis.

Case III (No. 374776). S. H., a female, aged twenty, was admitted on December 19, 1934, and discharged January 3, 1935. Following the delivery of a child four months before admission, the patient was seized with a severe colicky pain in the right upper quadrant, radiating to the back. Similar attacks occurred weekly and were associated with chilliness, nausea and vomiting. Between the attacks, there were frequent digestive disturbances, aggravated by the ingestion of fried or fatty foods.

Examination revealed an obese female with some tenderness and spasm in the right upper quadrant.

Cholecystography showed the gallbladder to be well outlined. It was of moderate density, emptying well after a fatty meal, and there was no evidence of gallstones.

Operation disclosed a markedly distended gallbladder with a large amount of thick dark bile and a number of very small stones within the gallbladder and in the cystic duct. The cystic duct was dilated. There were a number of recent adhesions of omentum to the wall of the gallbladder.

The pathological report showed chronic cholecystitis.

Case IV (No. 318173). C. S., a male, aged fifty-five, was admitted on September 8, 1930, and discharged on October 8, 1930. He gave a two-year history of epigastric pain occurring at irregular intervals. Three days before admission, he was seized with a severe attack of epigastric pain, which was relieved only for a short period by morphine. There were no other symptoms.

On physical examination, the abdomen was held rigid. There was tenderness in the epigastrium, and to the left, and percussion tenderness at the back at the level of twelfth thoracic and first lumbar vertebra. The white blood count was 10,000, with 77 per cent polymorphonuclears. The picture was that of an acute pancreatitis. The patient was observed for sixteen days. The chief symptoms, however, subsided within four days after admission. The gastrointestinal roentgen series was reported as negative. Examination of the gallbladder showed it to "fill and empty with dye. The proximal portion appears to be unchanged, and the fundus appears to be adherent to the hepatic flexure. No stones are demonstrated. These findings are not certain." The Rehfuss test showed a free acid of 0 and a total acid of 10. In spite of the roentgen findings, a diagnosis of chronic cholecystitis and cholelithiasis with chronic pancreatitis was made.

Operation revealed a thickened gallbladder with numerous small calculi, and one large calcium bilirubinate stone. The gastrocolic omentum was opened and several white areas suggestive of fat necrosis were spread over the pancreas. A cholecystectomy was performed. The pathological report showed chronic cholecystitis and cholelithiasis. The postoperative course was uneventful.

Case v (No. 397186). C. K., a female, aged forty-four, was admitted on August 15, 1936, and discharged on September 6, 1936. She gave a history of having had typhoid fever thirty-six years ago, an appendectomy twenty years ago, and a hysterectomy eight years ago. Three years ago, she suffered her first attack of right upper quadrant pain, radiating to the back. Two years ago, this recurred and since then she has had similar episodes at intervals of three to four months. The patient states that jaundice was noted during the last attack. Roentgenograms were taken and the report was that the gallbladder was normally visualized, and there was no evidence of biliary calculus.

Physical examination disclosed some tenderness in the right upper quadrant.

She was roentgenographed again upon admission. Examination of the gallbladder by means of a Graham test showed the viscus to be normal in size, shape, filling and emptying time, with no evidence of gallstones.

While under observation, the patient had occasional episodes of right upper quadrant pain. In view of this, exploration was performed which was entirely negative. During convalescence, the patient continued to have the same type of pain as before operation. It was felt that this might be explained by dyskinesia of the sphincter of Oddi. The patient was discharged for medical care.

She was readmitted on November 17, 1936, stating that five weeks before her second admission, she had another attack of sharp right upper quadrant pain radiating to the back, and lasting for several hours.

Physical examination revealed a scar in the right upper quadrant with local tenderness and slight spasm.

At operation, the gallbladder appeared externally normal but there was a small cholesterin stone in the cystic duct three-quarters of an inch above the common bile duct. The common bile duct was explored and no calculi were found. Drainage of the common bile duct was instituted, and cholecystectomy performed. The patient ran an uneventful course. Pathological report showed chronic cholecystitis. The follow-up has been satisfactory.

The reasons for the apparently normal roentgen findings in these 5 cases, in which frank gross pathology was present, are difficult to explain. It is likely, however, that the pathology did not interfere materially with the physiological activity of the organ, although the inflammatory process appeared sufficiently advanced to cause symptoms. These symptoms, however, do emphasize one point, which is important. If the clinical history is as typical as it was in these cases, exploration should be proceeded with in spite of normal findings as revealed by the Graham test.

Cholelithiasis was present in 4 of these 5 cases. In Case i, there was a small stone in the neck of the gallbladder. In Case iii, there were innumerable small stones, and one in the cystic duct. In Case iv, there were several small and one rather large calcium bilirubinate stone, and in Case v, there was a calculus in the cystic duct. It is readily conceivable that small stones, especially those in the cystic duct, might easily be obscured by a dense gallbladder shadow.

2. *Cases in Which There Was Normal Filling and Emptying of the Gallbladder, and in Which Radiopaque and Radiotranslucent Shadows Were Present.* There were 38 cases in this group. Four were reported as showing either filling or emptying defects, in addition to the presence of radiopaque and radiotranslucent shadows. While all these cases showed some degree of cholecystitis, it was not particularly marked in a gross pathological sense, and the lesion had probably not advanced sufficiently to interfere seriously with the concentrating power of the gallbladder. Calculi were present in 36 patients, although the wall of the gallbladder showed some thickening in 18 cases. There were only 2 in which pericholecystitic adhesions of recent origin were noted. Yet in spite of this, 23 of these patients suffered from episodes of colic and other symptoms for over a year, 6 less than one year, and more than three months, and 8 less than three months.

The one patient, Case vi, in which gallbladder disease did not appear to be present, revealed a duodenal ulcer. Subsequent examinations, however, made the diagnosis of an additional cholecystitis more than likely.

Case vi (No. 569822). A male, aged fifty-one, was admitted August 14, 1935, and discharged September 19, 1935. The patient was discharged six months ago from the Medical Service with a diagnosis of coronary arteriosclerosis. Since discharge, he has experienced pain in the right upper quadrant with vomiting and distention. There was definite relationship to meals, but patient was frequently awakened at night by the pain. There was no hematemesis, tarry stools, chills, fever or jaundice. For two years this pain has been severe, radiating to the left lower quadrant, and left interscapular region. There was also definite radiation down the left anterior chest and arm. Although there has been a loss of about 8 pounds in weight since discharge, his general health has been good, except when he suffered these episodes of severe pain. There was no dyspnea, orthopnea, edema or palpitation.

During investigation in the Out-Patient Department, two gastrointestinal series were done. The first showed a slight degree of prepyloric irregularity with the duodenal bulb complete, and the second showed prepyloric spasm with the duodenal bulb slightly irregular. The opinion of the roentgenologist was that there was a duodenal ulcer with prepyloric spasm. The gallbladder series showed the viscus to be normal in size and shape, but it contained radiotranslucent calculi.

Physical examination showed marked sclerosis of all palpable vessels. The blood pressure was 160/100. There was tenderness in the epigastrium, in the right upper and lower quadrant. This was most marked, however, in the right lower quadrant.

Operation disclosed a large indurated ulcer in the duodenum, adherent to the pancreas behind, and to the gallbladder anteriorly. The surrounding tissues were injected, indicating an acute inflammatory process. There were no stones palpable in the gallbladder. A typical no-loop gastroenterostomy was done.

The postoperative course was uneventful. However, re-examination of the gallbladder by the Graham test showed radiotranslucent shadows indicating the presence of stones.

The patient was subsequently admitted for interscapular pain, which was thought to be due to a spondylitis of the dorsal spine which roentgen examination verified.

3. Cases in Which There Was Poor Visualization of the Gallbladder Without Stone. There were 22 cases in which there was poor or faint visualization of the gallbladder after the oral administration of the dye. At operation 19 of these patients showed definite evidence of chronic cholecystitis, and 15 suffered from an additional cholelithiasis. In 8 there was an acute exacerbation of the disease, evident in the pathological examination. The gallbladder, which was dilated in 9, and contracted in 3 cases, was definitely adherent in 11 instances. Three of this group presented a carcinoma of the pancreas.

In spite of the roentgen findings, indicative of gallbladder disease, there were 3 cases in which the gallbladder was externally normal, although about one there were a few pericholecystitic adhesions.

Case vii (No. 337958). B. S., a female, aged thirty-six, was admitted April 27, 1932, and discharged May 26, 1932. The patient was in the hospital ten months previously with a five-day history of pain in the right lower quadrant, and vomiting. Her symptoms were thought to be due to gastroenteritis. Sigmoidoscopy at that time showed a mildly congested and granular mucosa, which was possibly thought to be due to a mild colitis. Her temperature was 100° F.; her pulse 100.

The patient was very hypersensitive and moderate tenderness was felt in the right lower quadrant with slight rebound tenderness. There were a few small internal and external hemorrhoids, and an anal fissure. The white blood count was 13,500, with 51 per cent polymorphonuclears. The gastrointestinal series was negative, the appendix was tender, but not fixed. The gallbladder series showed the viscus to visualize faintly with dye. There was no evidence of stones. The Wassermann reaction was negative. The urine was negative.

The hemorrhoids were first excised and the anal fissure cauterized, and subsequent abdominal exploration revealed a normal gallbladder and a few small uterine fibroids. An appendectomy was performed. The convalescence was uneventful. The pathological report showed chronic appendicitis with partial obliteration. The follow-up course was satisfactory.

Case viii (No. 335586). G. C., a female, aged fifty-four, was admitted February 23, 1932, and discharged March 6, 1932. At the

time of admission, she gave a history of having lost 30 pounds in weight. For three months she experienced indefinite epigastric pain, radiating to the right side without relation to meals. Two Graham tests were done, which showed only faint visualization of the gallbladder.

Operation disclosed a normal gallbladder. The appendix was found adherent subcecally by band in its mid-region. An appendectomy was performed. The postoperative course was uneventful. The follow-up was satisfactory.

Case ix (No. 375698). S. Z., a male, aged fifty-five, was admitted September 12, 1932, and discharged October 16, 1932. The patient gave a two months' history of very severe cramp-like epigastric pain, radiating to the right hypochondrium and back, but without nausea, vomiting or chills. The attacks occurred about twice a week and lasted from two to four hours.

Physical examination disclosed abdominal tenderness in the right upper quadrant. The white blood count was 20,400, with 73 per cent polymorphonuclears. The spinal fluid was negative. The gastric analysis was free hydrochloric 46, total, 56. A barium enema showed no evidence of any lesion in the gastrointestinal tract. Examination of the gallbladder showed faint visualization and no calculi.

An exploration was performed, which was completely negative.

The patient has been followed and still has vague complaints, although the pain in the back has disappeared.

These 3 cases are interesting in that the clinical history in the first 2 were certainly not typical of gallbladder disease in spite of the faint visualization of that viscus. Both these patients were completely relieved by appendectomy. The third case is still obscure.

The reason why a gallbladder should visualize faintly when the organ appears normal anatomically cannot be accounted for. It is barely possible that faulty roentgen technique may have been responsible for some of these errors.

4. *Cases in Which There Was Poor Visualization of the Gallbladder and in Which Radiopaque or Radiotranslucent Shadows Were Present.* There were 34 cases in this group, and exploration revealed definite cholecystitis in all, and an accompanying cholelithiasis in 31. There was definite thickening of the gallbladder in 22 of the cases, and although the gallbladder was described as normal in one case, it contained a stone in the cystic duct. Eleven cases of this group contained definite pericholecystic adhesions. Four of these cases were jaundiced at the time of admission, and 2 presented choledocholithiasis at operation.

5. *Cases in Which There Was no Visualization of the Gallbladder Without Stone.* This group constituted the greatest number of the cases in this series and consisted of 86 patients. Sixty-nine revealed stones, and there were 13 cases of non-calculous cholecystitis, of which 2 were accompanied by carcinomata. The gallbladder wall was thickened in 37 cases, and marked adhesions were present in 39, while in 23, the gallbladder was described as shrunken. Six of the cases were jaundiced at the time of admission, and of these, stones were present in the common duct in three. There were 4 cases in which the roentgen appearances were not verified by the operative findings. One was a case in which the gallbladder appeared externally normal, although there were a few pericholecystitic adhesions. Another was a duodenal ulcer, and in 2 the gallbladder was presumably normal.

Case x (No. 374883). B. H., a female, aged thirty-four, was admitted December 22, 1934, and discharged January 2, 1935. Four months prior to admission, the patient experienced symptoms of upper abdominal distention and belching after eating, which were aggravated by the ingestion of fatty and fried foods.

The physical examination disclosed an obese and well-developed female.

The gallbladder failed to visualize.

A laparotomy was performed under spinal anesthesia, which disclosed the gallbladder to be grossly normal, except for some adhesions to the stomach and omentum. The appendix was removed.

The follow-up results have been satisfactory.

Case xi (No. 348594). I. S., a male, aged fifty-three, was admitted February 1, 1933, and

discharged February 26, 1933. Four days before admission, the patient experienced an indefinite history of epigastric pain. Twelve hours before admission, there was severe epigastric pain radiating to the right upper quadrant.

Physical examination disclosed a diffuse tenderness over the right side of the abdomen and in the right costovertebral angle. The tenderness seemed most marked under the right costal margin. There was no obliteration of liver dullness.

The white blood count was 11,600, with 81 per cent polymorphonuclears. There was a temperature of 101° F. A flat film failed to reveal the presence of free air. Under conservative observation, the acute process subsided. A gallbladder series failed to visualize the viscus.

Operation revealed a perforated duodenal ulcer which had been sealed by an adherent gallbladder. The gallbladder was separated and the perforation was sutured. The patient postoperatively developed pneumonia of the right lower lobe but, following this, made an uneventful recovery. The patient was subsequently admitted for a partial gastrectomy.

The failure of the gallbladder to visualize in this case, even though it appeared grossly normal, could easily be explained by its adherence to a perforated duodenum, and the fact that its function was probably inhibited by the presence of an adjacent acute pathology.

Case XII (No. 332247). R. L., a female, aged twenty-four, was admitted on November 13, 1931, and discharged December 30, 1931. She gave a history of having had an appendectomy two years prior to admission. Since then she had had attacks of pain in the right lower quadrant. One year ago, the patient was operated upon for adhesions. She experienced the last severe attack of right loin pain associated with urinary symptoms one month before admission. The genitourinary and gastrointestinal roentgen series were negative. The gallbladder series failed to visualize *on two occasions*.

Physical examination showed the right kidney palpable. There was right lower quadrant and right costovertebral tenderness. A spastic cecum was felt. Cystoscopy was negative. The pyelogram was normal with the exception that the kidney failed to empty after twelve minutes with the patient in the reverse Trendelenburg position. The gastrointestinal series showed an extremely ptosed stomach with a small prepyloric incisure of the lesser curvature. Duodenum was normal, and the gastric mobility was delayed as well as that in the small intestine. Examination of the gallbladder with dye failed to visualize the viscus. On the basis of three gallbladder series failing to visualize, the patient was explored and the gallbladder found normal. The postoperative course was uneventful.

The patient has been followed for three years and still has persistent pain in the right lower quadrant.

The failure of the gallbladder to visualize on three separate occasions in this case is rather unusual. It is extremely doubtful, even if these repeated roentgen findings could be accounted for by physiological defect of the gallbladder, that the clinical symptomatology could be explained on this basis.

6. *Cases in Which There Was no Visualization of the Gallbladder, and in Which Stones Were Present.* There were 23 cases in this group, all of which revealed definite gallbladder pathology. There was a thickening of the gallbladder in 8, resulting in marked contraction in 6 cases. Marked pericholecystitic adhesions were present in 9 cases. Three of the gallbladders were carcinomatous. The one case in which stones were not present was a case of carcinoma of the head of the pancreas.

DISCUSSION

While the clinical history of repeated attacks of gallbladder colic with its characteristic radiation is invaluable in the diagnosis of cholecystitis and cholelithiasis, there are some cases in which the history is not as characteristic. The Graham-Cole method of oral cholecystography has proved of inestimable value, not only as yielding positive confirmatory evidence in the diagnosis of gallbladder disease, but has often served as a sole means of arriving at a diagnosis in patients in whom the condition was not even suspected. Cholecystography is not 100 per cent perfect. There is no test which is, and in this series, checked by operation, it has been proved

to be 94 per cent correct. The error seems to be greatest in those cases in which there is either poor or faint visualization. In this group it was 13 per cent correct. It is less in those cases in which there is no visualization, being 4 per cent correct. Poor visualization, and no visualization of the gallbladder, accompanied by the direct or indirect evidence of calculus, may almost be taken as infallible evidence of positive surgical pathology, because, even though calculi were occasionally absent, marked evidence of cholecystitis was invariably present.

A normal visualization of the gallbladder by the dye, with normal filling and emptying in the presence of a definite history of cholecystitic disease, should not be taken as positive proof that the biliary passages are normal. The test, in a case of this nature, should be repeated because often a second examination will demonstrate definite abnormality. The following case is especially instructive in this regard.

CASE XIII (No. 342102). M. B., a female, aged forty, was admitted August 11, 1932, and discharged August 18, 1932. There was a three-year history of epigastric pain.

Physical examination disclosed an obese female. There was tenderness in the epigastrium. The urine was negative. The gallbladder series was negative. There was a hemoglobin of 60 per cent. Blood pressure was 100/60. Rehfuss test meal showed hypoacidity, and the guaiac test was negative. After a few days in the ward, the patient became asymptomatic. In view of the Rehfuss test meal findings and secondary anemia, it was felt that no gastric lesion was present. The patient was discharged for further study.

She was readmitted one month later with pain in the right upper quadrant of two days' duration. Physical examination revealed marked tenderness in the right upper quadrant. It was now felt that the patient was definitely suffering from gallbladder disease. A second gallbladder series showed faint visualization, containing a small radiotransparent shadow.

Laparotomy revealed a small elongated and slightly thickened gallbladder with several stones. The appendix and gallbladder were removed.

Pathological report showed an acute catarrhal appendicitis and chronic cholecystitis.

Occasionally, a second examination will present additional evidence of the disease which the previous test failed to disclose.

CASE XIV (No. 325289). I. Y., a male, aged thirty-two, was admitted April 25, 1931, and discharged May 24, 1931. The patient was roentgenographed nine months previous to admission and the gallbladder failed to visualize. The symptoms, however, were so transient, and the neurotic element was so great, that he was referred for medical treatment. He attended the Out-Patient Department for treatment and remained symptom-free until a week before his second admission. At this time he experienced an attack of right upper quadrant pain. The temperature was 102° F. There was slight spasticity and tenderness in the right upper quadrant. The temperature fell to normal within a few days and all symptoms disappeared. Roentgen examination showed that the gallbladder filled normally with dye but within were seen a large number of radiotransparent calculi.

Operation disclosed a normal appearing gallbladder with a number of small stones.

Pathological report showed chronic cholecystitis and cholelithiasis. The postoperative course was uneventful.

A critical review of the cholecystographic findings in relation to the pathology seen at the time of operation is disappointing. While the roentgen findings may be classified arbitrarily into the groups previously noted, no predictions or deductions can be made as to the surgical pathology of the gallbladder. While the microscopic report will invariably disclose a chronic cholecystitis, the actual degree of disease in the gallbladder will vary tremendously. Moreover, the involvement seems to bear little or no relationship to the severity of the symptoms. The visualization of the gallbladder appears dependent upon the ability of the liver to secrete sufficient amounts of the ingested dye, the patency of the cystic duct, and the physiological activity of the gallbladder to concentrate the dye. Impairment of any of these three factors may cause the organ to be poorly

or faintly visualized, or not to be visualized. The liver, even though diseased, being an organ with an enormous reserve capacity, usually secretes a sufficient quantity of dye, and under ordinary circumstances this factor may be eliminated as a primary cause of non-visualization. It was not responsible for a single case in this series.

The cystic duct does not play as significant a rôle as might be imagined because in this group in which the gallbladder visualized normally, the lumen of the cystic duct occasionally was partially occluded by a calculus. On the other hand, in the majority of cases in which visualization of the gallbladder was either poor or deficient, the cystic duct was usually patent and the gallbladder contained bile. As a matter of fact, in 137 cases proved by operation, the cystic duct contained a calculus in only 17 instances. The inference is obvious. Cholecystography, as originally stated by Graham, is more of a gauge of physiological activity than an index of degree of pathological involvement.

The diagnosis of cholelithiasis is certainly enhanced, and its probabilities augmented by this test, because although radiotransparent and radiotranslucent shadows are not always indicative of stones, calculi were present in 51 of the 57 cases which presented roentgen evidence of calculosis. Many of these were cholesterin stones previously invisible with ordinary technique, but now rendered diagnostically possible through the mediation of negative shadows.

There still seems to be a widespread prejudice against the administration of the dye in the presence of jaundice, although this has been denied by many.[1] If the dye does not seem to increase the toxicity of the jaundice state, its use should be extended in cases of icterus. It may prove, according to Foote and Carr,[1] a positive means by which the jaundice due either to an intra- or an extrahepatic block may be differentiated. If the Graham test is not used during the jaundiced state in obscure cases, it is especially indicated when the icterus clears. It may save subsequent embarrassment. The following case, which may or may not have been a toxic hepatitis on the first hospital admission, was certainly a case of cholelithiasis on the second admission. The roentgen findings in this case, and certainly in others of a similar nature, are of interest.

Case xv (No. 378065). A. M., a male, aged thirty-six, was admitted March 25, 1932, and discharged April 28, 1933. The patient was first admitted in February, 1932, because of jaundice associated with anorexia and dizziness. He had been previously treated for lues, although the Wassermann reaction was negative on admission. Under observation, the jaundice cleared spontaneously, and it was assumed that it was due to hepatitis, secondary to arsphenamine or syphilis. The patient remained well for about a year. One day before the second admission, he was seized with a sudden acute epigastric pain radiating to the left lower quadrant, followed by nausea and vomiting.

Physical examination disclosed marked tenderness in the epigastrium, with the sensation of a mass. The temperature was 102° F. The white blood count was 31,000, with 70 per cent polymorphonuclears. The temperature soon fell to normal. The Wassermann reaction was negative. The gallbladder series revealed the viscus to be rather small but normal in shape, filling and emptying time, but within its contour a large number of small stones were seen.

Operation revealed a moderately thickened gallbladder which contained numerous small stones. A cholecystectomy was performed. The follow-up was satisfactory.

CONCLUSIONS

Oral cholecystography is of undoubted value not only as confirmatory in cases of cholecystitis and cholelithiasis, but as a sole diagnostic means in which early cholecystitis has not been suspected.

In a series of 208 cases, checked by operation, the roentgen diagnosis of gallbladder disease was correct in 94 per cent. The error was greatest in those cases in which there was either faint or poor visualization without stone, but the test was infallible in

those cases in which there was either faint, or no visualization of the gallbladder with evidence of calculosis.

If the clinical history of gallbladder disease is unquestionable, surgical exploration is indicated, even in the presence of a normal Graham-Cole test, but a repetition of the test may add additional information.

There is evidently no definite correlation between the roentgen findings and the surgical pathology at the time of operation. The test seems to be a gauge of physiological activity rather than an actual index of the degree of pathology involved.

Oral cholecystography, inasmuch as the dye does not seem to increase the toxicity of the jaundiced state, should be extended to cases of icterus in which a differential diagnosis cannot be made between intra- and extra-hepatic block.

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REGIONAL JEJUNITIS*

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SINCE the excellent article by Crohn and his collaborators[1] on the syndrome of regional ileitis, many additional reports of this disorder have appeared in the literature. Brown and his associates[2] observed that the ailment might occur at any point along the intestinal tract, the clinical picture varying with the site of the lesion. Included among their 18 cases were 3 cases of jejunitis. Kantor's[3] description of the roentgenological findings has greatly facilitated the diagnosis of the disease. Because of its rather infrequent occurrence, roentgen studies in jejunitis have not received the same attention. The following report is submitted in the hope that with additional reports, roentgenologic criteria for diagnosis of jejunitis will be as well established as they have been for ileitis.

REPORT OF CASE

The patient, a Greek male, aged forty-four, was admitted to the hospital because of epigastric pain and vomiting. The onset of his present illness was four days before admission when he began to experience cramp-like pain in the epigastrium, associated with nausea and vomiting. The pain and vomiting came directly after every meal and were of such a disturbing nature that the patient refrained from eating food for four days. The vomitus was noticed to be very dark in color. There was no diarrhea. Diabetes had been discovered one year ago and during the present illness polydipsia and polyuria were prominent symptoms. Of additional interest was a purpuric eruption over the lower extremities, noted first, ten days before admission and which subsequently remained unexplained.

Examination on admission revealed an undernourished, dehydrated man, free from pain. The vital signs were not abnormal. The abdomen was soft and nontender. The skin over both lower extremities was covered with multiple small purpuric areas. The blood count showed 10,500 white blood cells with 54 per cent polymorphonuclears and a hemoglobin of 75 per cent. A provisional diagnosis of diabetes with acidosis was made and was apparently confirmed by the finding of a marked glycosuria, acetonuria and a blood sugar of 305 mg. The acidosis was promptly controlled. Two days later the patient was again awakened by

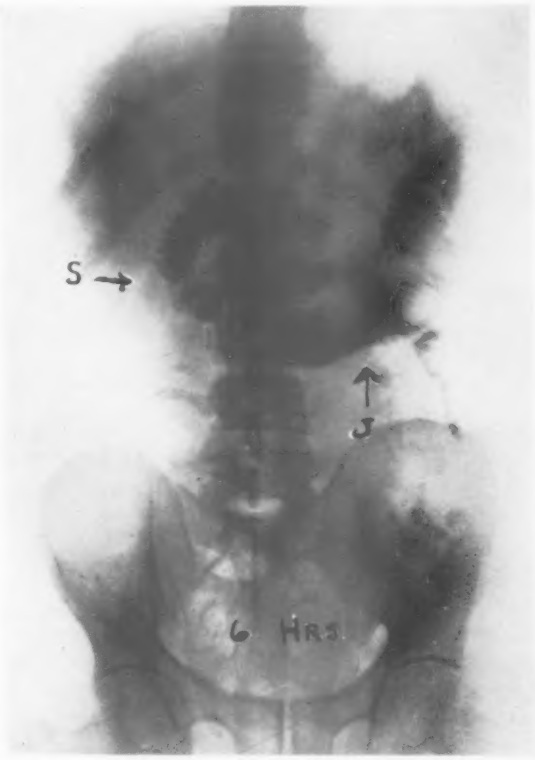

FIG. 1. Six-hour film showing stasis in the duodenum (*S*) and jejunum (*J*).

severe epigastric pain. There was no vomiting. The upper abdomen was tender and slightly distended. Temperature was 100.8° F. A blood count showed 25,000 white blood cells with 90 per cent polymorphonuclears. The urine was negative for sugar. The next day the patient was symptom-free. Thereafter there recurred many similar episodes, of varying duration, sometimes associated with almost intractable vomiting. The stools on occasion were tarry in color and gave a strongly positive reaction for

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FIG. 2. Film taken one-half hour after ingestion of meal showing marked distention of duodenum (*D*) and irregularity in filling of jejunum (*J*). Stomach (*S*) shows no defect.

blood. The temperature curve was an irregular one, ranging about 101° F., but at times ascending to 103° F. Roentgen study several days after admission showed that six hours after ingestion of the barium meal there was retention in the duodenum and upper coils of the jejunum (Fig. 1). Roentgenoscopic and roentgenographic examination of the stomach showed no abnormality. Further studies were done one week later. At this time a film taken approximately one-half hour after ingestion of the meal showed duodenal distention and gross irregularity in the filling of the upper coils of the jejunum (Fig. 2). The six-hour film this time showed gastric stasis and flecks of barium apparently caught in the mucosal folds of the jejunum (Fig. 3).

The diagnosis, however, was not apparent and exploration was performed by Dr. Kirby Dwight. At operation the upper portion of the jejunum and the adjacent part of the duodenum were found to be intensely red and thickened. The regional mesenteric lymph nodes were enlarged and succulent. A biopsy of one of these nodes was reported by the pathologist, Dr. Chester Brown, as hyperplastic lymphadenitis. No resection was performed. The postoperative course was uneventful and the patient was singularly free of abdominal symptoms for the rest of his stay in the hospital. He was discharged improved. Unfortunately he has failed to return to the follow-up clinic.

Comment. In retrospect it seems that the diagnosis should have been made prior to the operation. A fairly clear-cut syndrome seems to have presented itself: (1) severe epigastric pain; (2) vomiting; (3) evidence of bleeding in the gastrointestinal tract; (4) fever and mild leukocytosis; (5) absence of roentgen evidence of disease of the stomach and duodenum; (6) the positive roentgen findings noted above, viz., evidence of stasis and gross irregular defects in the upper intestinal tract.

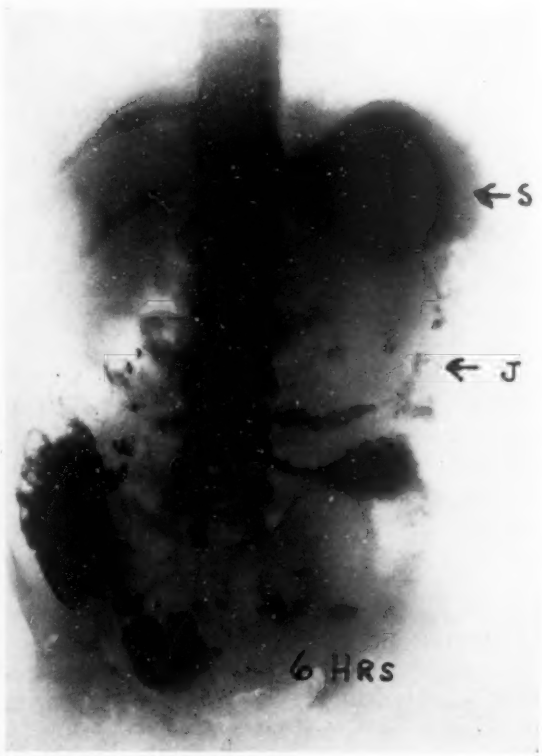

FIG. 3. Six-hour film showing stasis in stomach (*S*) and flecks of barium remaining in mucosal folds of jejunum (*J*).

The clinical picture apparently was well defined. However, the diagnosis was not suspected because of the rarity of the disorder.

The roentgen findings deserve further comment. Brown and his coworkers have stated that the roentgen manifestations of regional enteritis depend upon the nature of the pathological changes plus the superimposed functional disturbances of motility. In this case the pathological findings were purely inflammatory without evidence of fibrosis and stenosis. The somewhat variable roentgen findings indicate that they were partly due to deformity arising from inflammatory changes but more to the resulting disturbances in motility.

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LOCALIZED NONSPECIFIC ULCERATIVE ENTERITIS

WITH SOME UNUSUAL FEATURES

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THE recent emphasis laid by Chron, Ginzburg and Oppenheimer[1] on cases of ulcerative ileitis has been of interest to

FIG. 1. Case 1.

all roentgenologists. These lesions are being seen by all of us and a solid foundation for the recognition and treatment of them is already established. Because it is common knowledge that resection results in long periods of cure, the following cases and their outcome are deemed of value and worth recording.

REPORT OF CASES

CASE 1. B. K., husky male, aged forty, had had irregular fever, lower abdominal cramps and nausea for six weeks prior to examination in our office. There had been no localized pain or diarrhea. He was known to have had a duodenal ulcer with hemorrhage one year previous to this. The appendix had not been removed. A barium meal study was instituted at once with the finding of duodenal ulcer, ulcerative ileocolitis and *a normal colon from the hepatic flexure distalward* (Fig. 1). Five days later at laparotomy, the cecum and ascending colon were found to be thick-walled "and of a tuberculous appearance." The terminal ileum was adherent to the posterior peritoneum over a group of broken-down retroperitoneal lymph glands. In dissecting the thickened ileum free, an abscess cavity was entered filled with thick, yellow pus. The appendix was long and apparently involved in the "same tuberculous process." An appendectomy and drainage of the abscess were done and closure was made. One month later a fecal fistula developed which drained for six months. The abdomen was again opened, the terminal ileum, cecum and ascending colon were again found to be greatly thickened and hose like, and all of these structures were resected, anastomosis being accomplished between the ileum and transverse colon. The balance of the colon was of normal appearance. About a year and a half later the patient, having been well since his resection, suddenly had a severe melena. An immediate barium meal examination showed again the duodenal ulcer

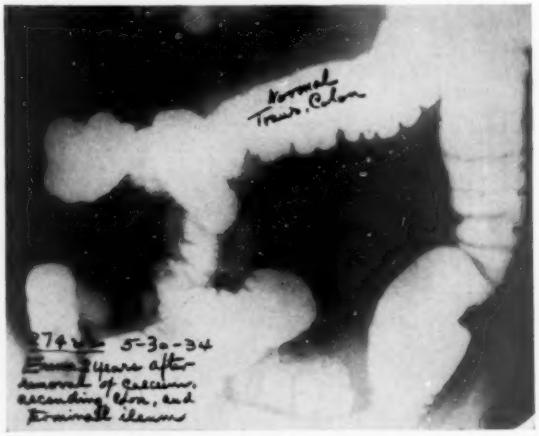

FIG. 2. Case 1.

[1] Chron, B. B., Ginzburg, L., and Oppenheimer, G. D. Regional ileitis; pathologic and clinical entity. *J. Am. M. Ass.*, 1932, *99*, 1323–1329.

previously seen *and a normally haustrated colon with no evidence of ulceration* (Fig. 2). The anastomotic area was seen to function satisfactorily and to be of normal outline and size. He was placed on medical regimen for peptic ulcer and did well in that he had no more hemorrhages nor any hunger pain. However, from this time on and up to the present writing he has had a gradually progressive diarrhea with three to four loose stools daily, moderate fever and abdominal cramps. A third barium study (enema only) done in the midst of this diarrheic period showed definite roentgen evidence of ulcerative colitis extending from the rectum and sigmoid to the midtransverse, the remaining proximal colon and ileum being of average appearance. In addition to the contracted, ahaustral, feather-edged border in the roentgen picture, there were multiple, round non-opaque spots in the barium-outlined colon which were considered to be polypi secondary to chronic ulcerative colitis. A proctoscopic examination showed ulceration in the rectum. At present the patient continues to have diarrhea, cramps and fever, but is not extremely ill. He is moderately anemic. The pathological report of the resected intestine showed ulceration in all three portions, i.e., ileum, cecum and ascending colon, the process being most intense in the colon. Numerous sections were cut for microscopical study from various areas and in none of these could evidence of a specific etiology be determined. The diagnosis was "nonspecific ulceration."

Comment. The feature of interest in this case is not that nonspecific ulceration was found in both small and large intestine for that has been described many times before, but that resection in a patient with nonspecific ileocolitis resulted in only temporary cure of short duration, and that this patient subsequently developed generalized ulceration throughout most of the colon. A review of the literature dealing with nonspecific ileitis and ileocolitis fails to yield a similar example.

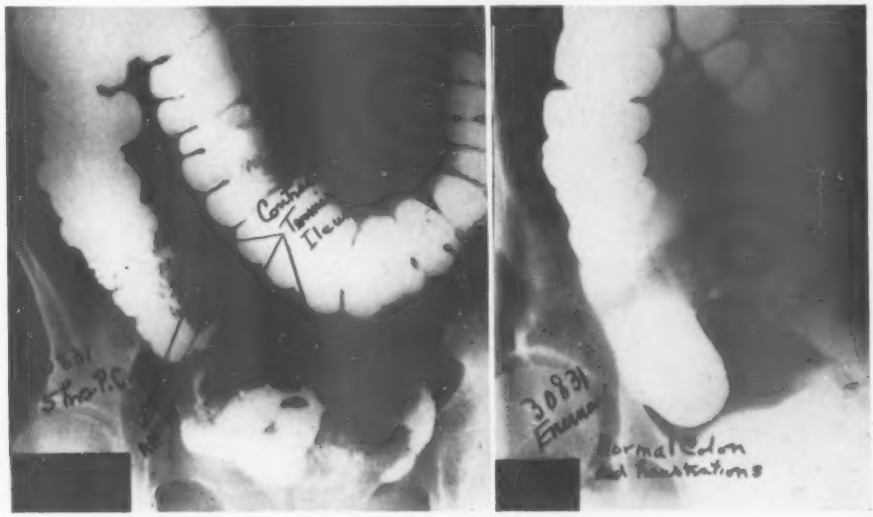

FIG. 3. Case II.

CASE II. H. A., a somewhat emaciated male, aged forty-seven, had had abdominal cramps for the past three weeks. The cramps began shortly after meals and lasted about an hour; they were moderately severe. The patient's temperature was elevated 1 or 2 degrees, he had a moderately elevated white count, a mild diarrhea, but no gross blood in the stool nor any abdominal tenderness. He stated that he had always been healthy until his present illness and was working when he presented himself for medical care. Digital examination revealed a mass anterior to the rectum and above the prostate which was fixed and seemed extracolonic in location. A barium meal study showed a narrow, irregular, irritable terminal ileum, which was not tender nor palpable as a mass through the abdominal wall (Fig. 3). The pathological change appeared to begin about 30 cm. above the ileocecal junction and extended downward to that structure. Close in-

spection of the barium-filled cecum and colon failed to reveal evidence of any abnormality. The colon margins were smooth, the caliber and haustra were average, and no sign of heightened irritability could be detected; the only irritable section of the gastrointestinal tract was the terminal portion of the ileum. At laparotomy, done under the diagnosis of regional ileitis, the hose-like, thickened terminal ileum was resected and anastomosis of the ileum to the cecum accomplished by means of a Murphy button. For three months the patient made an uneventful recovery—gained weight and strength and gave every indication of having been relieved of his disease. However, this state of affairs was short lived; he began to have loose stools with much mucus, not bloody at first; these increased in number from day to day, finally becoming uncontrollable, and in less than a month from the onset of the diarrhea he died—all efforts aimed at controlling his increased emaciation and diarrhea being of no avail. Post-mortem examination showed a tremendously severe grade of ulcerative ileocolitis (Fig. 4). The lesions began in the lower ileum, where there were many perforations, and involved the entire colon to such an extent that one could hardly find a single patch of mucosa left in the colon from cecum to rectum. Microscopically, there were no evidences of amebic infection, tuberculosis, or any specific infectious process. The organisms recovered were gram-negative bacilli. The pathological report on the terminal ileum, which had been resected at laparotomy four months before, corresponded in every way with the picture seen in the bowel following death. Cultures made on blood agar and brain broth at that time showed "no growth."

Fig. 4. Case II.

Comment. A case of localized or "regional" enteritis with nonspecific ulceration is described, which is again singular among reported cases, in that following resection of the diseased segment the patient went on to complete involvement of the colon and portions of the lower ileum.

CONCLUSIONS

Two cases of localized or "regional" nonspecific ulcerative enteritis are presented, which in their initial stages seemed to correspond to those described by Chron, Ginzburg and Oppenheimer, and others, but which failed to follow the orthodox path and were not cured by surgical resection. The conclusion, therefore, seems justifiable that the hitherto entirely optimistic surgical prognosis in these lesions should be more guarded in the light of the above case reports.

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A CASE OF CHRONIC ADHESIVE SPINAL ARACHNOIDITIS*

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ADHESIVE changes in the spinal meninges may be the result of many different causes, chief among which may be mentioned trauma, alcoholism, organic diseases, and senility. Low grade infections may also produce such changes in the membranes comprising the leptomeninx, and not infrequently, particularly after trauma, these adhesive changes may result in the formation of leptomeningeal cysts. The clinical manifestations in the presence of such meningeal changes would vary, depending upon the level or levels involved, but, generally speaking, the chief symptoms would be root pains, sensory changes, paralysis, mild evidences of cord compression, or at times even block.

This case is reported not because we consider it unique in any way, but merely because the roentgen findings were sufficiently well marked to permit of a fairly definite preoperative diagnosis.

The patient, a man aged fifty-five, gave an unimportant past history. He was always an active, outdoor man, used to hard work. The present illness began twelve years prior to his hospitalization, with pain in the region of the left scapula, which radiated to the neck, occiput, pectoral region, and down the left arm to the elbow. This pain gradually became almost constant and with no regressions, but at times there were exacerbations. Two years ago he strained his back pulling on a rope, and since then he has had pain in the right hip. At no time has there been staggering or localized weakness, but he has shown a band of hyperesthesia, beginning at the sixth thoracic segment on the left side and extending upward to the second thoracic; this was most marked anteriorly. A complete medical examination ruled out any general physical basis for the pain.

A careful roentgen examination of his spine failed to reveal any evidence of pathology. Later, after cisternal injection of lipiodol, more films were taken of the spine. This examination revealed the condition seen in Figures 1 and 2. From these films, it could be learned that there was no block because the oil descended to the terminus of the canal, but small, linear shadows

FIG. 1. Lipiodol may be seen in the upper thoracic region, deposited in such a manner that it casts shadows which are roughly linear, and placed horizontally.

can be seen in the upper thoracic region due to drops of oil evidently spread over portions of the meninges. Such a finding as an indication of an adhesive meningeal change is by no means original with us, but it was so well marked, and as it permitted us to make a rather definite differential diagnosis between tumor and leptomeningitis, the case seemed worth reporting.

At operation the condition illustrated in

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FIG. 2. Most of the oil may be seen in the terminus of the canal. Small residual droplets are seen adhering to the walls of the canal through the lower lumbar region.

Figure 3 was found. The cord was yellow and tough; the leptomeninges were thickened and seemed opaque. They were so adherent to the cord that they could not be opened in the usual manner, but rather piecemeal. There were many new blood vessels, but no real varicosities. A definite diagnosis of radiculitis and a chronic adhesive inflammatory process having been made, it was decided to perform a cordotomy. The patient had for some several months been taking large doses of morphine for the relief of pain. The widespread distribution of his radicular pains made cordotomy the operation of choice.

It was quite obvious at the operation why the original films of the spine showed no evidence of disease because there were no bony changes. The thickening of the involved membranes reduced the subarachnoid space and so made it comparatively easy for oil to lodge against thickened dentate ligaments, and subarachnoidal fibers, which are always comparatively large through the lower cervical and thoracic regions. These drops of oil do not lodge permanently in the locations seen in the films, but will eventually become dislodged and merge with the main body of the oil in the lower

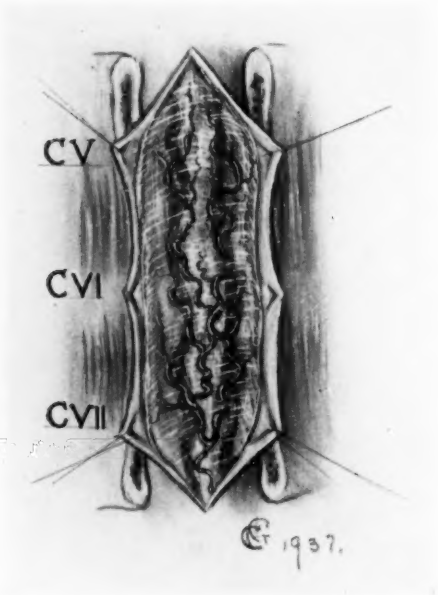

FIG. 3. The condition of the cord and meninges as seen at operation.

reaches of the canal. It is not at all uncommon for droplets of oil to remain scattered through the subarachnoid space after opaque oil injections, but the droplets will usually tend to retain a fairly globular shape, due simply to the fact that oil and water do not mix. But when the oil spreads over something more solid than spinal fluid, it is obvious that when viewed on edge it would cast a more or less linear shadow. This linear form of the shadow cast by the arrested oil droplets is the chief point of differentiation from droplets normally remaining after oil injection.

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ACROSCLEROSIS HYPERPLASTICA INTRAOSSEA

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THE question concerning the character of bone changes in scleroderma is by no means as yet solved, because different authors have been observing different pictures. It is possible that the etiological factor which determines the symptoms of scleroderma in every single case at the same time influences the character of the bone changes. As to etiology of scleroderma, there exist different theories. The advocates of the infection theory state that the predisposing factors can be erysipelas, tuberculosis, syphilis, leprosy, grippe or typhus. They believe also that often repeated cooling of the body and its drenching, or remaining for a long time in a wet and poorly lighted room can contribute to the development of the disease.

The adherents of the endocrine theory, as Curschmann,[1] speak about a disturbance in activity of the thyroid gland, suprarenal glands and ovaries; as proofs of which they mention cases of appearance of scleroderma during pregnancy or at the approaching of the climacteric age.

However, the most substantiated of all is the tropho-neurogenic theory put forward for the first time in 1895 by Lewin and Heller.[2] According to these authors, the functional derangement of vasomotor and trophic nerves, i.e., angio-trophoneurosis, is the cause of scleroderma. Apart from many clinical observations confirming this point of view, Kuré and his collaborators[3,4] have brought forth a series of exact pathologico-anatomic data. They state that in case of scleroderma universalis, the parasympathetic cells of the spinal cord and the parasympathetic fibers of the posterior roots of the spinal cord have a weaker development than is normally the case; in the parasympathetic fibers of the cutaneous nerves a distinct degeneration is noted, while the large middle myelin fibers remain almost intact. Thus, the Japanese authors attribute the cause of scleroderma to damage of the spinal parasympathicus, while Leriche and his school attribute it to the sympathicus.

We admit that in different cases different etiologic factors can contribute to the appearance of scleroderma. If in scleroderma the fingers are affected, it is called "sclerodactylia." Here the sclerodactylia is regarded as but a partial manifestation of scleroderma. This opinion was universally adopted before the appearance of the papers by Sellei.[5] According to this author, two quite different conditions are to be understood under the name of scleroderma: (1) true scleroderma, to which the diffuse, cordlike, flat as well as the circumscribed scleroderma belongs, and (2) acrosclerosis or the symmetrical progressive scleroderma of previous authors. This latter condition begins on the palm of the hand and causes more or less symmetrical changes of the fingers, much more rarely of the toes; the face is often affected to some degree.

Sellei describes the following characteristic bone changes: resorption, most sharply expressed in the distal sections of the phalanges and arthritic changes of type, arthropathia deformans or "pseudoarthritis deformans acrosclerosis."

Still earlier Paisseau, Laquerriére and Schérer[6] described certain analogous changes and summarized their observations as follows: intensive decalcification in the bones of the extremities, expecially in the phalanges with a tendency toward a slight deformation and disappearance of the joint spaces.

On the other hand, Livieratos and Tselios[7] did not see any bone changes in cases of sclerodactylia.

Of great interest are 3 cases of sclerodactylia described by Edeiken.[8] In two of

them, besides the phenomenon of atrophy of the end phalanges which gave the appearance of being amputated, there were calcium deposits in the soft tissue of the finger tips; in the third case, in addition to the typical phenomenon of atrophy, there was a sediment of calcium in the heads of the distal phalanges.

The chemical analysis of the deposits showed that they consisted of carbonates and phosphatic calcium.

In the case of scleroderma of the palms of both hands described by us (Fig. 1), a distinct interosseous deposit of calcium is observed in all the distal phalanges, and to a much smaller degree in the second and third phalanges. The soft tissues remain unchanged; in the joints no changes are to be seen; osteoporosis is not manifest. Thus our case, to our knowledge, is the second case to appear in the literature, the first one being published in the American literature by Edeiken.

FIG. 1. Acrosclerosis hyperplastica intraossea.

The first information about the calcium deposit in the soft tissues of the fingers in scleroderma was given by Scholefield and Webert[9] in 1911. In 1917 Olson[10] made similar observations and mentioned 8 additional cases taken from the literature; in these, besides the fingers, the above-mentioned deposits were also observed in other affected areas. Pollitzer[11] describes one case of scleroderma which was accompanied by a formation of a true bone in the soft tissues.

In the present case, the patient was a working woman, aged forty, whose occupation consisted in soaking yarn, her hands being almost continuously plunged into water. She complained of pains in the

hands and disagreeable sensations in the fingers such as at times a feeling of tenseness, again of stiffness and stitching. The roentgen diagnosis of sclerodactylia presents some difficulty if there is an osteoporosis of the phalanges without any calcium deposit. Then it is necessary to differentiate it from Cassirer's angiotropho-neurosis, from Buerger's disease (thrombo-angiitis obliterans), from Raynaud's disease, leprosy, neuro-derma-myositis (Figs. 2 and 3)* and syringomyelia. In such a case the diagnosis is made on the basis of clinical data. A specific feature in scleroderma, especially sclerodactylia, is

Fig. 2. Neuro-dermo-myositis, right hand.

the presence of calcium in the soft tissues of the finger tips with a simultaneous osteoporosis of the tips of the phalanges. The calcium deposit within the bone tissue of all phalanges of all the fingers in case of scleroderma is here described for the first

* As far as we know, it is here for the first time that the bone changes in this disease are described.

Fig. 3. Neuro-dermo-myositis, left hand.

time, because in Edeiken's case there were small deposits only in the distal phalanges. Further observations will show whether the changes are specific for scleroderma or whether they can also be observed in other diseases.

On the basis of the above given data, we propose the following classification of bone changes in scleroderma:

(1) Atrophic acrosclerosis (pseudo-arthritis deformans—Akrosklerose according to Sellei), characterized by osteoporosis of the bones of the extremities, especially of the distal phalanges, and sometimes by arthritic changes of the small joints;

(2) Hypertrophic acrosclerosis which can be of two types:

(a) Interstitial, characterized by osteoporosis of the distal phalanges and calcium deposit in the soft tissues of the finger tips, and

(b) Interosseous, characterized by the absence of osteoporosis in the bones of the extremities and by a calcium deposit in the bone tissue of all phalanges of both hands.

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THE PREVENTION AND TREATMENT OF ROENTGEN INJURIES OF THE SKIN

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THE best treatment of roentgen injuries is their avoidance. Irreparable injuries are an indication of some error in the technique of the treatment or of nonobservance of individual idiosyncrasies or of irradiation of a skin area damaged even slightly by a preceding radiation treatment. At times, severe skin lesions result from large radiation doses applied to deep-seated internal cancers, that could not be arrested by smaller doses. Prophylaxis means an intimate knowledge of the radiation dose, a careful general examination of the patient before treatment is applied and a careful history, especially regarding preceding irradiations and a knowledge of the factors observed in the treatment. Should one meet an injury, then a knowledge of the clinical symptoms and the treatment of radiation injuries are desirable.

Therefore, I shall consider, first, the influence of radiation quality, the time factor and the field size; second, the radiation reactions in the skin; and third, the treatment of radiation dermatitis and acute and chronic radiation ulcers.

THE INFLUENCE OF RADIATION QUALITY, TIME FACTOR AND FIELD FACTOR

The quality of the radiation influences the radiation dose and therefore the skin reaction. The discussion of the clinical history of skin changes will always refer to 200 kv. roentgen rays, a single application, a filter of 1 mm. Cu and a field size of 20 cm.[2]

Skin reactions differ depending on the physical factors employed in treatment.

The factors of roentgen therapy which must be known to determine the proper radiation dose and to avoid irreparable radiation injuries in the skin are the type of current and transformer, the voltage, the wave length; the half-value layer, the type of tube, whether air, water or oil cooled, and whether the walls are of thin or thick pyrex glass; the filter and its position within the radiation beam; the focus-skin distance; the size, the location, the direction and the number of fields; the dates, time intervals and duration of applications; the milliampere load, the number of roentgens applied to each field per treatment or per fraction; the diameters of the body portion which contains the growth; the size of the growth and its relation to the body surfaces on which the fields are placed. In this way the true topographical relations are obtained. The number of roentgens applied through each field and the percentage of the total depth dose and the total surface doses may then be calculated.

The quality of the roentgen ray in Ångström units is obtained from the percentage of absorption in 1 mm. copper and the graph shown in Figure 1, which gives the "apparently" average wave length. Such determinations can at best be only approximations. They are useful, however, if the permissible error is within the region of practical therapeutic application. The "apparently" average wave length may also be determined from the half-value absorption layer in copper. Table 1, which was constructed from the graphs of Figures 1, 2 and 3, gives all the factors necessary in applying roentgen rays therapeutically. The filter in deep roentgen therapy should be the equivalent of the half-value layer to attain the most homogeneous beam with the voltage used. The homogeneity could not be improved by additional filter material. I shall not go into any further discussion of the other factors, as they are self-explanatory. Exceptions are the determination of the single massive dose, the

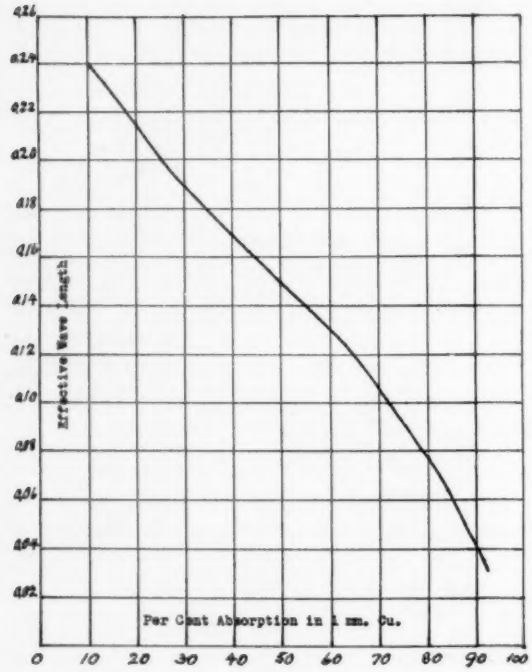

Fig. 1. Relation of absorption in 1 mm. copper to effective wave length.

proper spacing and timing of each fraction.

Since the investigations of Krönig and Friedrich in 1915, it is known that a measured radiation dose is better tolerated by

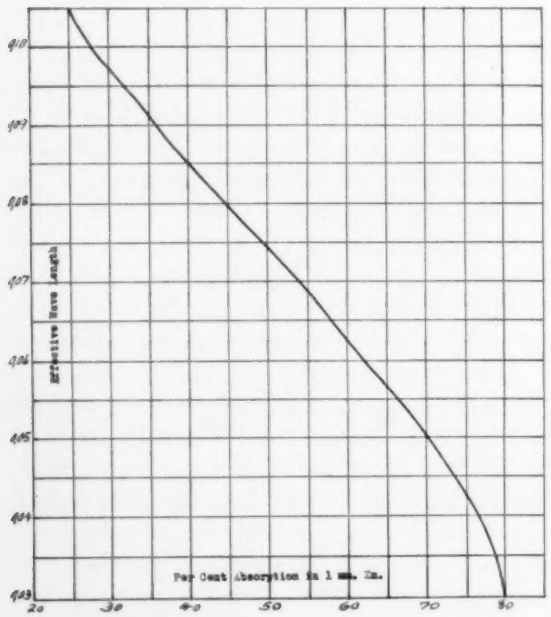

Fig. 2. Relation of absorption in 1 mm. zinc to effective wave length.

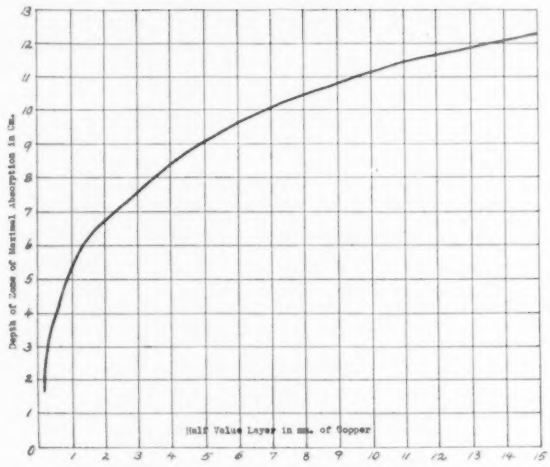

Fig. 3. Depth of zone of maximum absorption in relation to the half-value layer.

human tissue if it is administered in fractions over a long period of time than in a single dose. The greater the number of fractions, the more radiation can be delivered. Obviously the tissues recover to a certain extent in the intervals. This recuperation is not the same for all tissues, as found clinically. Many types of malig-

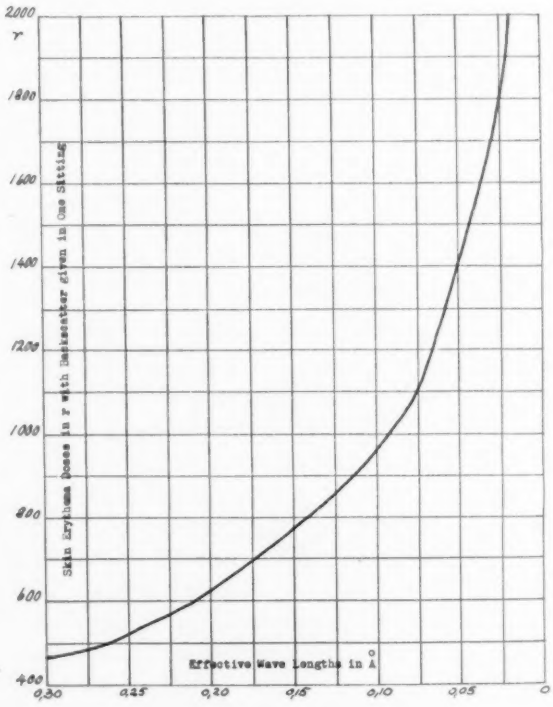

Fig. 4. Relation of skin erythema dose to effective wave length.

nant tumors regress after fractionated doses without marked permanent damage to normal tissues, whereas this is impossible with a single massive dose. This means that recuperation must proceed more rapidly in the normal than in the diseased tissues. Cumulation of radiation reactions can only occur if the spaced fractions are given during the latent period after the second day and up to the fifth day, the rate of recovery is about 25 per cent daily. For twelve days the residual effect progresses slowly up to 85 per cent and for twenty-seven days up to about 95 per cent. By the eleventh day there is only 15 per cent recovery and by the twenty-first day less than 10 per cent if daily fractions are given (Reismer). Of course,

Table I

RELATIONS OF HALF-VALUE LAYER IN MM. COPPER, KV., MAX., FILTER, λ EFF., SINGLE S.E.D. AND TEN FRACTIONAL S.E.D. DOSES FOR A FIELD OF 20 CM.²

Kv. Max.	Half-value Layer in mm. Cu	λ eff. in Å	Filter in mm.			S.E.D. with Back-scattering in r	
			Cu	Al	Sn	Single	Ten Fractional Doses
100	0.12	0.28	0.1	1.0		480	10×100
150	0.5	0.18	0.5	1.0		625	10×125
200	1.58	0.125	1.5	1.0		800	10×160
200	1.94	0.11	2.0	1.0		920	10×185
400	4.5	0.070	4.5	1.0		1150	10×230
500	5.0	0.056	5.0	1.0		1300	10×260
600	5.5	0.047	5.5	1.0		1400	10×280
700	6.0	0.040	6.0	1.0		1500	10×300
800	8.2	0.034	8.0	2.0		1700	10×340
				or			
			4.38	2.0	1.56		

before erythema, dermatitis or ulceration occur. The explanation must consider the "recuperation factor." Cumulation also takes place if the cell changes of the preceding radiation fractions are still present when the second radiation is applied.

The percentage of recovery or recuperation has been placed variously at 6 to 8 per day for 200 kv. roentgen rays, filtered with 0.5 mm. copper. Quimby et al., however, found that the recovery during the first twelve hours is about 50 per cent. It proceeds more and more slowly with increase in the number of fractions and intervals. This is due to the fact that the first radiation dose is applied to normal tissue and for all subsequent fractional applications the tissue has already undergone a certain amount of damage and the recuperation rate would be expected to be less. After the second fraction given on or the individual treatments must be less than the threshold skin doses.

When the single massive dose in value of skin erythema doses and roentgens with back-scattering is known, which for instance with 200 kv. and a field of 20 cm.² is 900 r, then the product of 900×0.2 gives the r dose, namely 180 r, for each fraction given every other day, ten times. If one decides to apply the tolerance skin dose which is 1,200 r with back-scattering with 200 kv. and a field of 20 cm.², then the product of 1,200×0.2 gives the r dose for each fraction, namely 240 r, which should be applied every other day, ten times. The final skin reactions are the same as those obtained with a single application.

If one changes the field size to smaller fields, then the number of roentgens must be increased as back-scattering is less and hence the roentgens should be increased to

TABLE II

FRACTIONAL TREATMENTS IN r WITH BACK-SCATTERING FROM 200 KV., 1.0 MM. CU FILTER AND A 20 CM.^{2} FIELD

Single Dose		Ten Fractions (One fraction applied every other day)
Skin tolerance dose	600	10×120 r
Skin erythema dose	900	10×180 r
Skin tolerance dose	1,200	10×240 r
Lethal dose	1,800–2,400	

The end reactions are the same for all methods. The dose ratios are 100:150:200:250.

obtain the same biological reaction or dose, according to Table III.

The determination of the factors given in Table I is not difficult. It requires the use of an r-meter and the graphs of Figures 1, 2 and 3. The percentage absorption occurring in 1 mm. of copper is measured. Figures 1, 2 and 3 give all the factors used in the construction of Table I, i.e. quality, filter, half-value layer and dose, the single massive and the fractionated small doses.

RADIATION REACTIONS IN THE SKIN

The point of attack of radiations in the human, and therefore the animal organism, is the cell. The action is usually centered in the chromosomes of the nucleus. It is most intensive during the metaphase of mitosis, which is the most radiosensitive period in the life cycle of the cell. A resting cell is usually more radioresistant. Depending on the radiation dose, the reactions produced in the skin vary. They are either reversible, conditionally reversible, irreversible or lethal.

In a reversible reaction, the action of the rays is of a transient nature. It produces a light erythema within fourteen to twenty-one days which disappears within twenty-one to twenty-eight days, leaving a discoloration of the skin behind, i.e. a mild tanning. The radiation dose that causes this reaction is the threshold skin dose which may be attained with 600 r with back-scattering from 200 kv. roentgen rays filtered with 1 mm. copper and applied over a field 20 cm.^{2} The skin reaction is of a transient nature and terminates in a complete anatomical and biological recovery. Re-irradiation may be given with impunity.

In the conditionally reversible reaction, the action of the rays produces changes which apparently disappear entirely from an anatomic standpoint but leave behind a biologically inferior tissue. A marked erythema, with scaling of the superficial cells of the epidermis appears within fourteen to twenty-one days, which gradually changes to a pronounced tanning. As long as the tanning persists the tissue is anatomically and biologically weakened. However, within a shorter or longer period the discoloration may fade gradually leading to a complete restitution. Should the same radiation dose be repeated while the tanning persists, then the subsequent reaction will be much more severe than that following the first dose and may become irreversible. The radiation dose which causes this reaction is about 900 r, with back-scattering, applied in one sitting over a field of 20 cm.^{2} and filtered with 1 mm. copper. It is the skin erythema dose.

The irreversible reaction is caused by a dose producing lasting changes. Within fourteen days a dusky bluish erythema occurs; within twenty-one days a dermatitis ensues which is either dry or wet. The dry dermatitis is characterized by a desquamation of the surface layer of the corium. The wet dermatitis leads to a formation of vesicles, which secrete a serous fluid. As healing ensues, a deep brown discoloration of the skin occurs, which is permanent. Within a period of six to twelve months atrophy occurs with the formation of telangiectasis. The skin is permanently damaged. An added radiation treatment or exposures to sunlight or ultraviolet rays, or continued external irritation such as pressure may result in destructive changes in the skin in the form of brawny induration or ulceration. The roentgen dose to cause irreversible changes is 1,200 r, with back-scattering, applied in one sitting, fil-

tered with 1 mm. copper and a field of 20 cm.^{2}. It has been termed the skin tolerance dose. Exceeding this one massive dose will lead to irreparable skin lesions.

The lethal skin reaction causes destructive skin lesions, namely the acute roentgen ulcer. Following the erythema and brown pigmentation, occurring within fourteen days, vesicles form which terminate in sharply limited, punched out ulcers which are very painful, within twenty-eight days. The fate of the ulcer is variable. It may remain stationary, become torpid and sluggish, or undermine adjacent tissues and finally terminate in the formation of heavy scar tissue on a basis of extensive destructive lesions. Keratoses frequently form. Roentgen cancers may follow these chronic lesions in from four to fourteen years. The cancers may be solitary or multiple. Metastases occur by way of the lymph stream in about 25 per cent of the cases. Recoveries are rare. The roentgen dose, applied in one sitting over a field of 20 cm.^{2} and filtered with 1 mm. copper, is 1,800 to 2,400 r with back-scattering.

Constitutional idiosyncrasies and variations in reaction depend on the region of the body surfaces exposed to irradiation. The sensitivity of the skin increases from the head down; the ankle skin is most radiosensitive. Surfaces of the body subjected to pressure show a more intense reaction; hence, the posterior surface reacts more intensely. Skin folds subjected to perspiration and maceration, such as the axilla, the folds beneath the breast, the abdominal skin folds in Hängebauch, the nates or, genital folds, are very radiosensitive. The light-complexioned skin is more sensitive than the dark.

Constitutional states accompanied by increased radiosensitivity are: the skin of a child; it is less resistant to the action of rays than the skin of the adult; endocrine disturbances, such as hyperthyroidism, the thymolymphatic state, diabetes mellitus, vagotonia among others. Acute psoriasis, lupus and acute eczema cause the skin areas to become much more sensitive.

Table III

IMPORTANCE OF BACK-SCATTERING FOR SIZE OF ENTRANCE FIELD MEASURED ON THE SURFACE

Size of Entrance Field	Depth of Phantom	Intensity	r with Back-scattering
20×20 cm.	30 cm.^{2}	100.0%	900
15×15 cm.		95.0%	945
10×10 cm.		87.0%	1,035
5× 5 cm.		77.0%	1,125
1× 1 cm.		66.6%	1,215

The histological changes observed in a first degree or reversible reaction are seen in the most radiosensitive part of the skin, i.e. the basal cells of the corium. This accounts for the practical absence of erythema, for the mild tanning and for the rapid regression of the skin to normal. The action is therefore merely functional or biological, as microscopic changes are almost never seen.

In a second degree reaction, inflammation and epilation are seen. The nuclei of the cells of the basal layer of the corium degenerate. This is only temporary. In a third degree or irreversible reaction, exfoliation or desquamation of the skin epithelium, due to radiation destruction, is seen. The desquamation may remain dry, or vesicles may form. The epithelization proceeds slowly and may be accomplished within four to eight weeks. Changes in the capillary vessels are pronounced. The glands of the skin become permanently destroyed which leads to a dryness of the skin. In a fourth degree or lethal reaction, acute roentgen ulcers form, due to a destruction of the epidermis and cutis by necrosis. The ulcer has either a tendency to heal slowly or does not heal at all. The basal cell layer of the skin is severely and at times totally damaged. If it becomes totally damaged, then epithelization cannot occur except from the non-irradiated basal cell layer in the periphery of the field. The ulcers are very painful. The tendency to slow healing or persistence of the ulcer results from the necrosis and the marked vascular changes involving the corium and

subcutis. The deep changes are produced with highly filtered, hard roentgen rays. Low voltages produce rather superficial lesions. The former are characterized by an involvement of the subcutaneous fascia. Hence the ulcer moves with the fascia or muscle layer. The superficial ulcers can be moved over the fascia. Edema of the skin may occur with the early reactions and is, as a rule, not permanent.

The late changes are brawny induration which appears after a latent period of two to twelve months. It involves the entire epidermis and subcutaneous fatty tissues or it may include the subcutaneous fascia and muscles. Telangiectasis is seen in the atrophic roentgen dermatitis. Latent scars with necrosis or chronic ulceration are the most severe late reactions and follow primary fourth degree reactions or repeated radiations with skin erythema or skin tolerance doses.

TREATMENT

The treatment of roentgen dermatitis should be expectant and conservative. Meddlesome therapy produces more harm than good. Rest in bed, avoidance of external pressure, sun bath of the entire body but with exclusion of the radiation areas, ointments (Edison ointment, Röntgensalbe) are preferable to lotions and powders. They should be applied lightly so as to maintain skin function. Soap, water, poultices, hot stoops or hot pads should be avoided. Castor oil applied lightly, morning and evening, gives excellent service in the lighter forms of dermatitis.

The treatment of acute and also chronic roentgen ulcers consists in rest in bed and avoidance of external pressure. The use of soap, water, hot applications and pads must be interdicted. The pain should be relieved by internal and never local medication: aspirin, pyramidon, phenacetin, veronal, sulfonal, trional and finally, in intractable instances, alkaloids of opium. However, with perseverance and good judgment, the use of opiates may be avoided. The dermatitis surrounding the ulcers may be treated with ointments. Wet applications of normal saline solution or infusion of chamomile for an hour at a time twice a day are recommended. Recently the leaves of aloes have been applied over such lesions. The results are claimed to be almost astounding. Maceration of the skin should be avoided absolutely. Scarlet red added to the ointments may stimulate repair. It is never advisable to attack ulcers surgically if the ulcer involves the entire skin and subcutaneous fat. This is usually seen after irradiations with short or hard roentgen rays. If soft roentgen rays were used, then the ulcers may be curetted. Should granulations form, then skin grafts may be done.

The treatment of roentgen cancers is radical excision with the regional lymph nodes. Procrastination is to be condemned.

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THE EFFECT OF GAMMA RADIATION ON MITOSIS*

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With the technical assistance of Geoffrey Keane, M.D., and Kathryn Hooper, A.B.

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THOUGH there is general agreement that cells in mitosis are more sensitive to irradiation than resting cells,[1,8] widely divergent views are held as to how mitosis is affected. In part, these views diverge because of differences in the test objects used, in part because of variation in type and quantity of radiation. Table 1, from Colwell[3], shows some of these discrepancies.

TABLE I

SENSITIVITY OF VARIOUS STAGES OF MITOSIS TO RADIATION

(Colwell)

Author	Date	Most Sensitive Phase	Material	Type of Radiation
Mottram	1913	Metaphase	*Ascaris* ova	Radium β and γ
Regaud	1923	Prophase Anaphase	Various tissues including neoplasms	X-rays and radium
Holthusen	1921	Metaphase	*Ascaris* ova	X-rays
Alberti and Politzer	1923–6	Metaphase	Cornea of salamander larva	X-rays
Strangeways and Hopwood	1926	Prophase	Tissue cultures Choroid and sclerotic of chick embryo	Radium and X-rays
Vintemberger	1928	Telophase	Ova of *Rana fusca*	X-rays
Love	1931	The sensitivity o a cell =a function of its displacement from maturity	Tissue cultures Choroid and sclerotic of chick embryo	X-rays

Once mitosis has begun it generally carries through to completion regardless of the type of agent used to inhibit it, although exceptions to this have been noted.[7] As one way of finding the most sensitive phase of mitosis, I have determined the frequency of the various stages of cell division in Walker carcinoma No. 256 after gamma irradiation.

METHODS

Walker carcinoma No. 256 in the Sloniker strain of white rat was used because extensive study in this and other laboratories has shown it to be fairly steady in growth rate and the malignancy to be high. Rats three to four months old, with subcutaneous tumor grafts of about fourteen days' growth (rarely eight days) amounting to about 5 c.c. in volume, were irradiated by surface application to the skin over the growth of from 2,100 to 2,500 mc-hr. of radon given over a period ranging from four and a half to five hours. Glass and steel tubes were placed in a cylindrical applicator with a wall of 2 mm. of brass, silver plated, the type commonly used in these hospitals for intracervical applications, and covered with thin rubber. The animals were killed at intervals after irradiation of the tumor, the mass excised, fixed in Zenker's fluid, sectioned, stained with phloxine methylene blue, and a differential count of mitoses made. The counts were made on from 10 to 20 sections from

* From the Laboratories of Pathology, Huntington Memorial and New England Deaconess Hospitals and The Department of Pathology, Harvard Medical School. Read in part before the American Society for Experimental Pathology, Washington, D. C., March 26, 1936.

various portions of the tumor, avoiding regions of necrosis.

From 15,000 to 24,000 cells were counted, and the number and stages of mitoses noted. The counts were made at a magnification of 900 diameters and questionable forms studied under higher power.

for a moderate preponderance of cells in metaphase. Within one and a half hours of the onset of irradiation a sharp drop in the number of mitoses occurs, reaching its nadir in the time interval from one and a half to ten and a half hours later.

As this drop in mitotic activity occurs,

TABLE II

STAGES OF MITOSIS AS INFLUENCED BY IRRADIATION
(*Expressed in number per 1,000 cells*)

Time hr.	Prophase	Metaphase	Anaphase	Telophase	Unclassified	Total
1	13.6	7.0	2.9	1.5	1.4	26.4
1½	2.2	4.0	1.5	0.6	1.8	10.1
3⅔	0.7	0.2	0.3	0.1	0.3	1.6
5	2.0	0.6	0.6	0.2	0	3.4
5½	0.3	0.1	0.1	0.1	0.4	1.0
7	0.2	0.1	0.1	0.1	0.1	0.6
7½	0.3	0.3	0.1	0	0.1	0.8
9	0.3	0.1	0.1	0	0.5	1.0
9½	0.4	0.2	0.2	0	0.3	1.1
10	0.5	0.3	0.4	0	0.1	1.3
11	0.2	0.1	0.1	0	0.3	0.7
11	2.0	10.0	3.0	2.8	1.8	19.6
11½	0.2	0.1	0	0.1	0.1	0.5
12	0.1	0.1	0	0	0	0.2
12	0.1	0	0	0	0.1	0.2
12⅔	8.7	2.4	2.8	2.5	3.7	20.1
14⅔	1.2	1.3	0.4	0.1	1.0	4.0
16½	6.8	1.8	2.0	1.6	0	12.2
23	0.3	1.5	0.5	0.1	0.2	2.6
24½	3.0	2.1	1.3	1.4	2.1	9.9
28½	4.8	2.1	1.2	1.3	0.6	10.0
30	1.7	4.2	1.1	0.7	1.1	8.8
38	2.5	1.5	1.6	0.3	2.6	8.5
48⅓	5.1	2.3	2.4	1.7	5.9	17.4
49	1.0	4.0	1.0	0.6	0	6.6
51⅔	3.4	1.6	1.6	0.7	3.9	11.2
74	0.7	3.5	1.0	0.7	0.4	6.3
Control	4.0	6.7	4.6	3.1	2.0	20.4

Some stages of mitosis could not be classified positively, and these were placed in the unknown group.

RESULTS

The data obtained are presented in Table II. In the non-irradiated tumor, about 20 mitoses occur per 1,000 cells, and are fairly evenly divided as to stage, except

the proportion of cells in prophase tends to rise, then falls about twenty hours after cessation of irradiation. Since the rise of prophases is only proportionate and actually a marked decrease in number occurs, the probability is that certain mitoses do not progress to completion owing to death of the cell or arrest of karyokinesis. However, as the numbers of cells in mitosis are

very small and some of the figures so abnormal as to defy classification, not much stress can be laid on this point.

Since a piling up of numerous mitoses does not occur at any one stage, since the reduction in total number occurs promptly, and since the reduction in number appears in all stages at about the same time, we may assume that the earliest steps in mitosis are inhibited, probably even before the visible changes of prophase can be noted.

If the figures may be accepted at their face value, beginning recovery from irradiation is signalized by relatively numerous prophases as would be expected had block occurred at a closely preceding stage.

Appearance of abnormal mitoses (multipolar spindles, lagging chromosomes, etc.) is not helpful, since they occur not infrequently in non-irradiated tumors of this type and since there is marked variation in both their absolute and proportionate frequency.* Table III illustrates this variability.

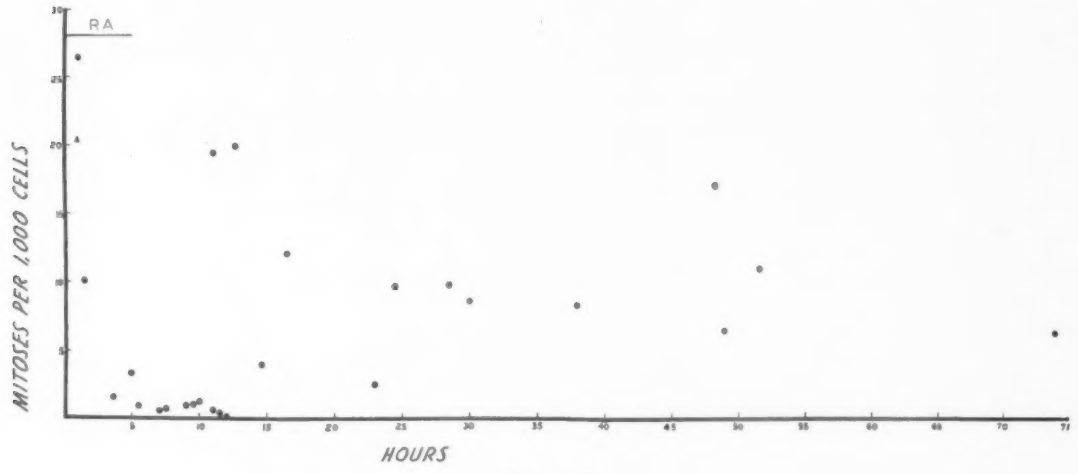

Chart I

Table III

FREQUENCY OF ABNORMAL MITOSIS IN IRRADIATED TUMOR TISSUE

Time hr.	Number per 1,000	Percentage of Total	Time hr.	Number per 1,000	Percentage of Total
1	4.6	17.4	12	0.1	50.0
1½	4.7	46.5	12⅔	4.5	22.4
3⅔	0.4	25.0	14⅔	1.9	47.5
5	0.2	5.9	16½	0.08	0.66
5½	0.4	40.0	23	1.9	73.1
7	0.1	16.7	24½	6.1	61.7
7½	0.4	50.0	28½	1.05	10.5
9	0.5	50.0	30	5.1	58.0
9½	0.6	54.5	38	6.1	71.7
10	0.6	46.2	48⅓	5.97	34.3
11	0.3	42.8	49	3.5	53.0
11	10.2	52.1	51⅔	4.8	42.9
11½	0.1	20.0	74	4.5	71.4
12	0.1	50.0			

* Owing to a pair of unusually long chromosomes, partial failure of separation at anaphase is often simulated.

DISCUSSION

While variation in types of biological material and of radiation leads to wide differences of opinion as to the most sensitive stage of mitosis, the present experiments indicate it to be the onset of prophase. This is in accord with the findings of Strangeways and Hopwood[9] on cultures of normal tissue irradiated by roentgen rays, of Love[5,6] on similar material and of Kemp and Juul[4] who subjected chick fibroblasts in tissue culture to radon.

That not all mitoses are inhibited is brought out by Table II, showing that malignant cells like normal cells[2] vary markedly in their susceptibility to irradiation. It might be objected that since sections were taken from different portions of the tumor these variations may be due to the rapid drop in effective dosage with distance, although the dose was sufficiently large to affect the most distant part. To further control this point, experiments with roentgen irradiation at 180,000 and 400,000 volt intensity are now being carried out.

CONCLUSIONS

1. Radon does not differ essentially from roentgen radiation in its effect on mitosis.

2. The premitotic phase is most sensitive to irradiation by radon as shown by the arrest of mitosis in Walker rat carcinoma No. 256.

3. The drop in mitotic count occurs rapidly during the first five hours after onset of irradiation and the count returns toward normal, though usually remaining lowered, about seven hours later.

4. Results here obtained with tumor grafts are similar to those with tissue culture material reported by others.

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THE EFFECT UPON THE PERCENTAGE DEPTH INTENSITY OF INCREASE IN VOLTAGE, FILTRATION AND SKIN-TARGET DISTANCE (150–300 KV. (PEAK))*

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IT HAS long been evident that there is little reason to believe we can cure or control many of the tumors that occur at a depth with less radiation than has been found necessary for the destruction of cancer of the skin. We are all familiar with the complications that arise when we attempt to deliver quantities of radiation into the deeper tissues that are in some measure comparable to the dosages that are employed on the surface. As far as the purposes of deep therapy are concerned, we believe that the effectiveness of any beam of radiation depends upon the proportion of its energy that can be delivered into (and is absorbed within) the depths of the lesion. While it is recognized that the practical limitations of such increases have not been established, we feel that better results are to be expected in deep roentgen therapy when we use the longest skin-target distance, the heaviest filtration and the highest voltage it is economically feasible to employ.

In any evaluation of different qualities of radiation we consider it is essential that we distinguish between "depth dosage" and expressions of depth intensity. It is usually considered that the former term refers to the amount of radiation reaching a depth in proportion to the quantity which applied to the skin produces a certain degree of erythema. As far as the lesion is concerned, we think of the "depth dose" as one, two or even three or more erythema doses, depending upon the number of portals used and the percentage of the dose applied to each portal which penetrates to the depth of the tumor tissue. On the other hand, for the purposes of the data herein reported, we have employed the term "percentage depth intensity" as an expression of the relative intensity of a beam of roentgen rays when measured at a given depth compared to the intensity of the same radiation as it strikes the surface of the overlying medium. We believe that the use of this term involves no consideration of biological effects and the fact that there is little appreciable difference between the percentage depth intensities of 200 and 300 kv. (peak) when both are filtered by "optimal" thickness of copper should not be regarded as evidence that the depth dosage is the same in both cases. Our own observations indicate little difference in the appearance of an erythema produced by 900 r at 200 kv. (peak) (0.75 mm. Cu) and one produced by 1,200 r at 300 kv. (peak) (2 mm. Cu), when both are given at an intensity of 15 r per minute. While our own figures indicate that the percentage depth intensity at 10 cm. is approximately 50 per cent when a skin-target distance of 80 cm. is employed in each case, due to the fact that the skin tolerates larger quantities of the harder radiation, we consider that the "depth dosage" with the 300 kv. (peak) is at least 25 per cent higher than can be obtained with the use of the 200 kv. roentgen rays.

The problems of the "economics of dosimetry" were originally presented by Failla and Quimby[1] in 1923. Their conclusions were made applicable to the conditions of therapy at that time and their studies have been continued in the more recent reports of Failla[2] and his coworkers in 1933, and by Quimby, Copeland and Woods[3] in 1934.

* From the Tumor Clinic of Drs. E. C. Padgett and F. C. Helwig, Kansas City, Missouri.

Moreover, the relative effects of various thicknesses of copper filter upon the percentage depth dose have been studied by Thoraeus, Mayneord and Roberts,[5] Quimby and Marinelli,[9] as well as by Taylor and Tucker[10] in 1933. However, we have found it interesting to determine the combination of filtration and distance which produces the highest percentage depth intensity that can be obtained with deep therapy equipment employing voltages of 150 to 300 kv. (peak). Originally we were merely interested in an attempt to determine the most efficient set-up for this particular machine; but in certain instances the results were rather surprising and we have decided to submit these data for the consideration of others who may also be interested in a comparison of the depth intensities obtained with various thicknesses of copper filter within this voltage range.

Apparatus and Experimental Procedure. The equipment used consisted of a 400 kv. (peak) (voltage doubling, Villard circuit) installation with a steel and lead overhead drum enclosing the therapy tube. With this arrangement, designed solely for deep therapy, the minimum skin-target distance is 70 cm. The roentgen tube used was a General Electric type XPT-3 and at the time of this experiment the tube and equipment had been in operation at 300 kv. (peak) (8–10 ma.) for more than ninety hours. We had previously observed that the relative intensities within a 10 cm. depth of normal (unembalmed) cadaver tissues showed considerable variation in the penetrability of different body areas, in close agreement with the recent observations of Quimby, Copeland and Woods.[8] Appreciating the practical advantages of a rice phantom as described by Pettit and Landauer,[7] we had a large phantom constructed for the use of rice in a somewhat similar manner. The wooden walls contained no metal and were so constructed as to correspond at all depths with a widening beam of radiation. The cross area of the phantom was made sufficiently large so that at all times the medium extended at least 10 cm. beyond the volume actually within the direct line of radiation. The phantom depth was 35 cm. so that measurements at a 15 cm. depth were taken over an underlying volume of medium 20 cm. thick. It was our belief that by the employment of a large phantom we could reduce to a minimum such errors as might result from wall effects and atypical scattering. To facilitate the accurate placing of the ionization chamber within the medium, holes were cut in the wooden wall and thin sleeve-like gauze guides were packed into the grain along the level of each depth at which measurements were desired. Surface intensity was measured with approximately half of the chamber's circumference pressed down into the grain. Somewhat to our surprise, we found the values as determined in wheat consistently nearer the figures obtained in cadaver tissues than were figures obtained when the same phantom was filled with rice. As a result of this observation we employed wheat as a phantom medium throughout the remainder of the experiments. In all instances the intensity of the radiation was determined by a standard Victoreen condenser type of small, portable chamber r-meter. All readings were taken at least twice, and the time was always made long enough to insure a loss of at least 50 per cent of the chamber's original charge. A 20×20 cm. portal and a skin-target distance of 80 cm. were used throughout this experiment, except when the skin-target distance is otherwise specified. There was no appreciable variation in the way all measurements were conducted and the entire experiment was carried out late at night when line voltage variations were rarely noted. A constant roentgen tube output was insured by close observation of a continuously reading ionization system that was built into the installation by T. R. Folsom,* and all the data comparing effects of varying the voltage, the amount

* We are also indebted to Mr. Folsom, physicist at the Lincoln General Cancer Clinic, for a determination of the copper absorption curves which have been employed in the calculation of our effective wave lengths (Duane 0.25 mm. copper method).

TABLE I

THE EFFECT UPON THE PERCENTAGE DEPTH INTENSITY OF INCREASING THE VOLTAGE FROM 150 TO 300 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 20×20 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
150	0	30.0 r/m / 100%	22.0 r/m / 73.3%	15.3 r/m / 51.0%	11.5 r/m / 38.3%	8.5 r/m / 28.3%	6.0 r/m / 20.0%	4.5 r/m / 15.0%
175	0	40.0 r/m / 100%	31.0 r/m / 77.5%	21.0 r/m / 52.5%	16.5 r/m / 41.3%	11.7 r/m / 29.2%	9.0 r/m / 22.5%	7.0 r/m / 17.5%
200	0	50.0 r/m / 100%	44.0 r/m / 88.0%	30.0 r/m / 60.0%	25.0 r/m / 50.0%	17.0 r/m / 34.0%	13.5 r/m / 27.0%	10.6 r/m / 21.2%
225	0	63.0 r/m / 100%	53.5 r/m / 84.7%	40.0 r/m / 63.5%	30.5 r/m / 48.4%	22.0 r/m / 34.9%	16.5 r/m / 26.2%	13.5 r/m / 21.4%
250	0	70.0 r/m / 100%	60.0 r/m / 85.7%	44.0 r/m / 62.8%	35.0 r/m / 50.0%	27.0 r/m / 38.6%	19.5 r/m / 27.8%	16.0 r/m / 22.8%
275	0	86.0 r/m / 100%	69.0 r/m / 80.2%	55.0 r/m / 63.9%	42.0 r/m / 48.8%	32.0 r/m / 37.2%	23.0 r/m / 26.7%	19.5 r/m / 22.7%
300	0	96.0 r/m / 100%	76.0 r/m / 79.2%	61.0 r/m / 63.5%	48.0 r/m / 50.0%	37.0 r/m / 38.5%	27.0 r/m / 28.1%	21.0 r/m / 21.8%

TABLE II

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 150 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25×25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
150	0	30.0 r/m / 100%	22.0 r/m / 73.3%	15.3 r/m / 51.0%	11.5 r/m / 38.3%	8.5 r/m / 28.3%	6.0 r/m / 20.0%	4.5 r/m / 15.0%
150	1 mm. Al	23.5 r/m / 100%	19.0 r/m / 80.8%	13.0 r/m / 53.3%	10.5 r/m / 44.7%	8.0 r/m / 34.0%	5.5 r/m / 23.4%	4.0 r/m / 17.0%
150	5 mm. Al	14.0 r/m / 100%	12.0 r/m / 85.7%	8.7 r/m / 62.1%	7.5 r/m / 53.6%	5.3 r/m / 37.9%	4.0 r/m / 28.6%	3.0 r/m / 21.4%
150	0.25 mm. Cu	12.0 r/m / 100%	10.5 r/m / 87.5%	8.0 r/m / 66.6%	6.7 r/m / 56.3%	5.0 r/m / 41.6%	3.7 r/m / 30.8%	2.5 r/m / 20.8%
150	0.50 mm. Cu	7.7 r/m / 100%	6.7 r/m / 87.1%	5.3 r/m / 68.7%	4.5 r/m / 58.1%	3.5 r/m / 45.2%	2.5 r/m / 33.8%	2.0 r/m / 25.8%
150	0.75 mm. Cu	5.5 r/m / 100%	5.0 r/m / 91.5%	4.0 r/m / 72.7%	3.3 r/m / 60.0%	2.5 r/m / 45.4%	2.0 r/m / 36.3%	1.7 r/m / 30.9%
150	1 mm. Cu	4.3 r/m / 100%	4.0 r/m / 93.0%	3.3 r/m / 7.67%	2.7 r/m / 62.8%	2.0 r/m / 46.5%	1.7 r/m / 39.5%	1.3 r/m / 30.2%

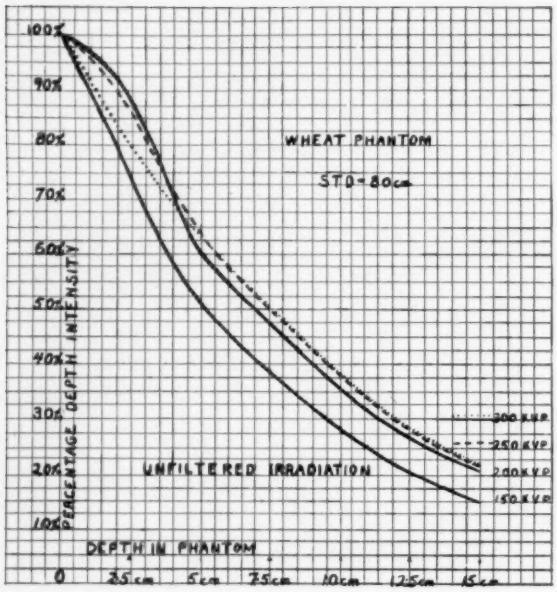

Fig. 1. Shows the absorption curves of unfiltered radiation as determined in the wheat phantom.

of filter, and the skin-target distance were made during one continuous period of tube operation.

Depth Intensities with Increasing Voltage: 150 to 300 kv. (peak). The first factor we were interested in was the effect upon the percentage depth intensity of increasing the voltage from 150 to 300 kv. (peak). Table I shows the relative intensities of the unfiltered radiation at varying depths in the wheat phantom. In a comparison of the 200 and 300 kv. (peak) radiation, it will be noted that while there is very little increase in the percentage depth intensity at depths greater than 7.5 cm., at the higher voltage there is a noticeable decrease in the relative intensity registered at a depth of 2.5 cm. These same differences in the distribution of radiation energy, as portrayed by relative intensities at varying depths, are also shown in Figure 1. In this graph the curves of only four voltages are shown because of the fact that the differences are small, even when the voltage is increased in steps of 50 kv. (peak). Few conclusions can be drawn from these findings, but it is evident that without proper filtration there is little improvement in the percentage depth intensity as the peak voltage is increased from 200 to 300 kv. (peak).

Depth Intensities with Increasing Filtration: 0.25 mm. to 5 mm. Cu.* In view of the evident importance of filtration, we have made an effort to determine just how much copper filter can be used to advantage as far as the percentage depth intensity is concerned. From absorption curves (Fig. 2), it is known that the first increases in filter rapidly harden a beam of radiation, but that after the greater proportion of softer rays are filtered out additional thicknesses of filter produce only slight additional improvement in the quality of the rays. In the data recorded in Tables II–VIII it will be noted that as additional thick-

* The copper filters used showed the following slight variations in thickness, i.e. (1) 0.25 mm. Cu was actually 0.254 mm. Cu; (2) 0.5 mm. Cu equaled 0.508 mm.; (3) 1 mm. Cu filters measured 1.01 mm.

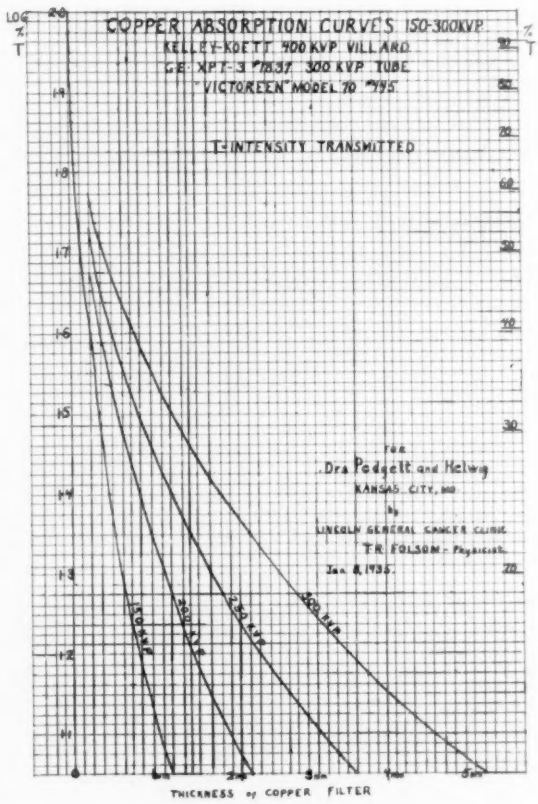

Fig. 2. Shows the copper absorption curves that were employed for the determination of the effective wave lengths (Duane 0.25 mm. copper method).

TABLE III

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 175 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25×25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
175	0	40.0 r/m / 100%	31.0 r/m / 77.5%	21.0 r/m / 52.5%	16.5 r/m / 31.3%	11.7 r/m / 29.2%	9.0 r/m / 22.5%	7.0 r/m / 17.5%
175	1 mm. Al	32.0 r/m / 100%	26.7 r/m / 83.4%	19.0 r/m / 59.4%	15.5 r/m / 48.4%	11.3 r/m / 35.3%	8.5 r/m / 26.6%	6.6 r/m / 20.6%
175	5 mm. Al	21.5 r/m / 100%	18.3 r/m / 85.1%	13.5 r/m / 62.8%	11.5 r/m / 53.5%	8.3 r/m / 38.6%	6.7 r/m / 31.2%	5.0 r/m / 23.3%
175	0.25 mm. Cu	18.5 r/m / 100%	16.0 r/m / 86.5%	12.5 r/m / 67.6%	10.5 r/m / 56.8%	8.0 r/m / 42.3%	6.3 r/m / 34.5%	4.5 r/m / 24.3%
175	0.50 mm. Cu	12.7 r/m / 100%	11.0 r/m / 86.6%	9.0 r/m / 70.8%	7.5 r/m / 59.1%	6.0 r/m / 47.2%	4.5 r/m / 36.2%	3.5 r/m / 27.5%
175	0.75 mm. Cu	9.3 r/m / 100%	8.5 r/m / 91.4%	6.7 r/m / 72.0%	5.7 r/m / 61.3%	4.5 r/m / 48.4%	3.5 r/m / 37.6%	2.7 r/m / 30.0%
175	1 mm. Cu	7.5 r/m / 100%	7.0 r/m / 93.3%	5.7 r/m / 76.0%	4.7 r/m / 62.6%	3.7 r/m / 49.3%	3.0 r/m / 40.0%	2.3 r/m / 30.6%

TABLE IV

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 200 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25×25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
200	0	50.0 r/m / 100%	44.0 r/m / 88.0%	30.0 r/m / 60.0%	25.0 r/m / 50.0%	17.0 r/m / 34.0%	13.5 r/m / 27.0%	10.6 r/m / 21.2%
200	0.25 mm. Cu	27.0 r/m / 100%	24.0 r/m / 88.9%	18.5 r/m / 68.5%	16.0 r/m / 59.3%	11.5 r/m / 42.6%	9.2 r/m / 34.1%	7.5 r/m / 27.8%
200	0.50 mm. Cu	19.0 r/m / 100%	16.7 r/m / 88.0%	13.3 r/m / 70.0%	11.3 r/m / 59.5%	9.0 r/m / 47.4%	7.0 r/m / 36.8%	5.7 r/m / 30.0%
200	0.75 mm. Cu	14.0 r/m / 100%	12.5 r/m / 89.3%	10.0 r/m / 71.4%	8.7 r/m / 62.1%	7.0 r/m / 50.0%	5.5 r/m / 39.3%	4.3 r/m / 31.4%
200	1 mm. Cu	12.0 r/m / 100%	11.0 r/m / 91.7%	8.7 r/m / 72.5%	7.5 r/m / 62.5%	6.0 r/m / 50.0%	4.7 r/m / 39.1%	3.7 r/m / 30.8%
200	1.5 mm. Cu	9.0 r/m / 100%	8.3 r/m / 92.2%	6.5 r/m / 72.2%	5.7 r/m / 62.7%	4.5 r/m / 50.0%	3.7 r/m / 40.5%	2.7 r/m / 30.0%
200	2 mm. Cu	7.0 r/m / 100%	6.5 r/m / 92.8%	5.0 r/m / 71.4%	4.3 r/m / 61.4%	3.5 r/m / 50.0%	2.8 r/m / 40.7%	2.3 r/m / 30.7%

TABLE V

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 225 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25 × 25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
225	0	63.0 r/m 100%	53.3 r/m 84.7%	40.0 r/m 63.5%	30.5 r/m 48.4%	22.0 r/m 34.9%	16.5 r/m 26.2%	13.5 r/m 21.4%
225	1 mm. Cu	16.5 r/m 100%	14.7 r/m 89.1%	12.0 r/m 72.7%	10.0 r/m 60.6%	8.0 r/m 48.6%	6.5 r/m 39.4%	5.0 r/m 30.0%
225	1.5 mm. Cu	12.0 r/m 100%	11.0 r/m 91.7%	8.7 r/m 72.5%	7.5 r/m 62.5%	6.0 r/m 50.0%	4.7 r/m 39.1%	3.7 r/m 30.8%
225	2 mm. Cu	9.5 r/m 100%	8.7 r/m 91.5%	7.0 r/m 73.6%	6.0 r/m 63.2%	4.7 r/m 49.4%	3.7 r/m 39.0%	3.0 r/m 31.6%
225	2.5 mm. Cu	8.0 r/m 100%	7.5 r/m 93.8%	6.0 r/m 75.0%	5.0 r/m 62.5%	4.0 r/m 50.0%	3.2 r/m 40.0%	2.5 r/m 31.3%
225	3 mm. Cu	6.7 r/m 100%	6.3 r/m 94.0%	5.0 r/m 74.6%	4.3 r/m 64.2%	3.3 r/m 49.2%	2.7 r/m 40.3%	2.0 r/m 30.0%

nesses of filter are employed the increases in the percentage depth intensity only roughly parallel the degree of improvement in the quality of the radiation. Moreover, it is obvious that any increase in the relative depth intensity resulting from a hardening of the rays by the addition of more filter can be accomplished only by the loss of a considerable proportion of the original intensity of that particular beam of

TABLE VI

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 250 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25 × 25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
250	0	70.0 r/m 100%	60.0 r/m 85.9%	44.0 r/m 62.7%	35.0 r/m 50.0%	27.0 r/m 38.6%	19.5 r/m 27.9%	16.0 r/m 22.9%
250	1 mm. Cu	22.0 r/m 100%	20.0 r/m 90.9%	16.0 r/m 72.7%	14.0 r/m 63.6%	11.0 r/m 50.0%	8.5 r/m 38.6%	7.0 r/m 31.8%
250	1.5 mm. Cu	16.7 r/m 100%	15.5 r/m 92.8%	12.3 r/m 73.7%	10.7 r/m 64.1%	8.3 r/m 49.9%	6.5 r/m 38.9%	5.3 r/m 31.7%
250	2 mm. Cu	14.5 r/m 100%	13.0 r/m 90.0%	10.5 r/m 72.4%	9.0 r/m 62.1%	7.3 r/m 50.4%	5.7 r/m 39.3%	4.5 r/m 31.0%
250	2.5 mm. Cu	11.5 r/m 100%	10.7 r/m 93.0%	8.5 r/m 73.9%	7.3 r/m 63.4%	5.7 r/m 50.0%	4.7 r/m 40.9%	3.5 r/m 30.4%
250	3 mm. Cu	10.5 r/m 100%	9.7 r/m 92.4%	7.5 r/m 71.4%	6.7 r/m 63.8%	5.3 r/m 50.4%	4.3 r/m 40.9%	3.3 r/m 31.4%

radiation. It is well to remember that as the radiation is hardened by additional thicknesses of filter there is very little gain in the percentage depth intensity to compensate for this loss (of total radiation intensity) and that this apparent inefficiency becomes more evident as the thickness of the filter increases.

Depth Intensities with Increasing Skin-Target Distances: 70, 80, 90, and 100 cm. The one method of increasing the percentage depth dose which is universally available is the use of a greater skin-target distance, but a major disadvantage is the rapid loss of radiation intensity as the focal distance is increased. Figure 3 shows the improvement in the percentage depth intensity at depths of 5, 10 and 15 cm. when the distance is changed from 70 to 100 cm. in 10 cm. steps. The most interesting findings in this regard come from an estimation of the efficiency of this method of increasing the percentage depth intensity. As similar figures could be prepared for the relative efficiency of increasing

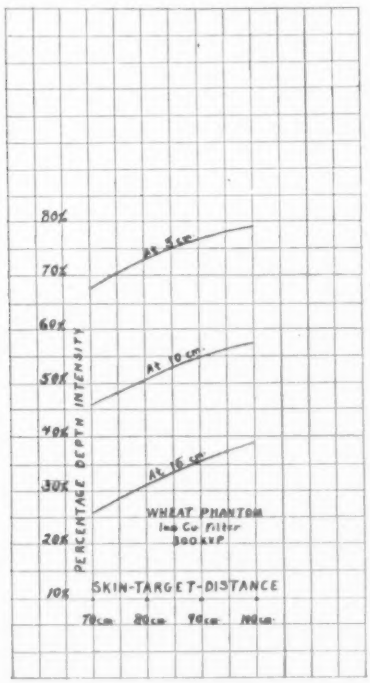

Fig. 3. Shows the improvement in the percentage depth intensity as the skin target distance is increased.

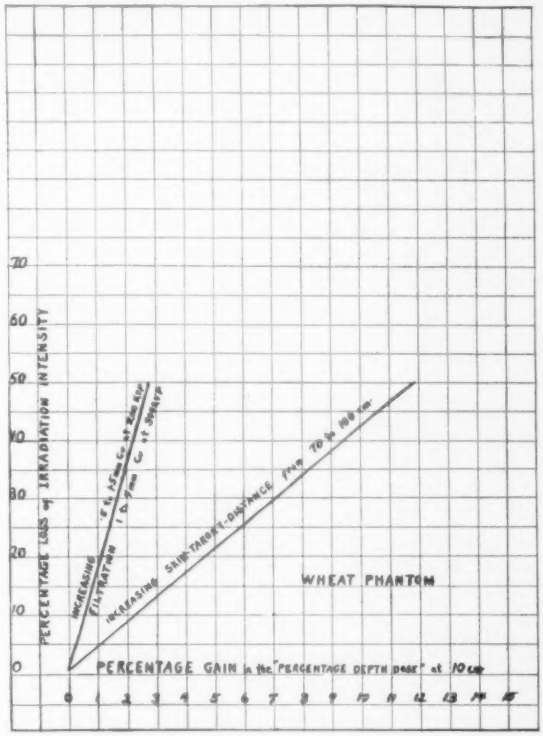
PERCENTAGE LOSS of IRRADIATION INTENSITY
INCREASING FILTRATION
INCREASING SKIN-TARGET-DISTANCE
WHEAT PHANTOM
PERCENTAGE GAIN in the "PERCENTAGE DEPTH DOSE" at 10 cm

Fig. 4. Shows that as far as the percentage depth intensity is concerned it is more efficient to increase the skin-target distance than to harden the radiation by the use of additional thicknesses of copper filter.

thicknesses of filter, it was evident that a comparison of the two should yield information of practical value to the radiation therapist.

Previous studies have also reported the greater efficiency of increasing the skin-target distance as compared with attempts to improve the relative intensity at a depth by the employment of additional thicknesses of copper filter. The advantage of the former procedure is particularly evident if we consider the relative gain in the percentage depth intensity when equal proportions of the original radiation intensity have been lost. In Figure 4, it will be noted that an increase in the skin-target distance from 70 to 100 cm. results in a loss of approximately 50 per cent of the available radiation energy; but the percentage depth intensity at a 10 cm. depth is 11.8 per cent higher at the longer dis-

TABLE VII

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 275 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25 × 25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
275	0	86.0 r/m 100%	69.0 r/m 80.2%	55.0 r/m 64.0%	42.0 r/m 48.8%	32.0 r/m 37.2%	23.0 r/m 26.7%	19.5 r/m 22.7%
275	1 mm. Cu	27.0 r/m 100%	23.5 r/m 87.0%	20.0 r/m 74.1%	17.0 r/m 63.0%	13.3 r/m 49.3%	10.5 r/m 38.9%	8.3 r/m 30.7%
275	1.5 mm. Cu	20.5 r/m 100%	18.5 r/m 90.2%	15.5 r/m 75.5%	13.0 r/m 63.4%	10.5 r/m 51.2%	8.7 r/m 42.4%	6.7 r/m 32.7%
275	2 mm. Cu	19.0 r/m 100%	17.0 r/m 89.5%	13.9 r/m 72.1%	12.0 r/m 63.2%	9.7 r/m 51.0%	8.0 r/m 42.1%	6.3 r/m 32.6%
275	2.5 mm. Cu	15.5 r/m 100%	14.0 r/m 90.3%	11.7 r/m 75.4%	9.5 r/m 61.3%	8.0 r/m 51.6%	6.5 r/m 41.9%	5.0 r/m 32.2%
275	3 mm. Cu	13.0 r/m 100%	11.5 r/m 88.4%	9.5 r/m 73.0%	8.0 r/m 61.5%	6.5 r/m 50.0%	5.3 r/m 40.7%	4.0 r/m 30.8%

TABLE VIII

THE EFFECT OF INCREASING FILTRATION UPON THE PERCENTAGE DEPTH INTENSITY AT 300 KV. (PEAK)

Kv. (peak) at 8 ma.	Filter	Portal = 25 × 25 cm.				S.T.D. = 80 cm.		
		Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
300	0	96.0 r/m 100%	76.0 r/m 79.2%	61.0 r/m 63.5%	48.0 r/m 50.0%	37.0 r/m 38.5%	27.0 r/m 28.1%	21.0 r/m 21.9%
300	1 mm. Cu	32.5 r/m 100%	29.0 r/m 89.2%	24.0 r/m 73.8%	20.3 r/m 62.4%	16.5 r/m 50.8%	12.7 r/m 39.1%	10.3 r/m 31.7%
300	1.5 mm. Cu	27.0 r/m 100%	24.0 r/m 88.9%	19.7 r/m 73.0%	17.0 r/m 63.0%	13.7 r/m 50.7%	11.0 r/m 40.7%	8.7 r/m 32.2%
300	2 mm. Cu	23.5 r/m 100%	21.0 r/m 89.3%	17.0 r/m 72.3%	14.7 r/m 62.5%	12.3 r/m 52.7%	9.7 r/m 41.3%	7.7 /rm 32.8%
300	2.5 mm. Cu	18.7 r/m 100%	16.7 r/m 89.2%	14.0 r/m 69.9%	11.7 r/m 62.5%	10.0 r/m 53.4%	8.0 r/m 42.8%	6.3 r/m 33.6%
300	3 mm. Cu	17.0 r/m 100%	15.0 r/m 88.2%	12.0 r/m 70.6%	10.5 r/m 61.7%	9.0 r/m 52.9%	7.3 r/m 42.9%	5.7 r/m 33.5%
300	4 mm. Cu	13.0 r/m 100%	11.3 r/m 87.0%	9.0 r/m 69.2%	8.0 r/m 61.5%	7.0 r/m 53.8%	5.7 r/m 43.8%	4.3 r/m 33.1%
300	5 mm. Cu	10.5 r/m 100%	9.0 r/m 85.7%	7.3 r/m 70.0%	6.3 r/m 60.0%	5.5 r/m 52.4%	4.5 r/m 42.8%	3.5 r/m 33.3%

tance. On the other hand, increasing the filtration of 200 kv. (peak) from 0.5 mm. to 1.5 mm. of copper, or increasing the filtration of 300 kv. (peak) from 1 mm. to 4 mm. of copper results in a 50 per cent loss of the available radiation intensity; but in each case the use of the heavier filter when changing from 0.25 mm. to 0.75 mm. of copper than is noted when the filtration is increased from 1 mm. to 3 mm. of copper at the higher voltages in Tables V-VIII.

Depth Intensities with Decreasing Effective Wave Lengths: 0.225 Å to 0.075 Å. Having determined the effects on the per-

TABLE IX

PERCENTAGE DEPTH INTENSITIES FOR INCREASINGLY HARDER ROENTGEN RAYS

Quality of the Radiation	Portal = 25×25 cm.				S.T.D. = 80 cm.		
	Surface	2.5 cm.	5.0 cm.	7.5 cm.	10.0 cm.	12.5 cm.	15.0 cm.
0.225 Å eff. 150 kv. (peak) 0.25 mm. Cu	12.0 r/m 100%	10.5 r/m 87.5%	8.0 r/m 66.6%	6.7 r/m 56.3%	5.0 r/m 41.6%	3.7 r/m 30.8%	2.5 r/m 20.8%
0.200 Å eff. 150 kv. (peak) 0.50 mm. Cu	7.7 r/m 100%	6.7 r/m 87.1%	5.3 r/m 68.7%	4.5 r/m 58.1%	3.5 r/m 45.2%	2.5 r/m 33.8%	2.0 r/m 25.8%
0.175 Å eff. 200 kv. (peak) 0.50 mm. Cu	19.0 r/m 100%	16.7 r/m 88.0%	13.3 r/m 70.0%	11.3 r/m 59.5%	9.0 r/m 47.4%	7.0 r/m 36.8%	5.7 r/m 30.0%
0.150 Å eff. 200 kv. (peak) 1 mm. Cu	12.0 r/m 100%	11.0 r/m 91.7%	8.7 r/m 72.5%	7.5 r/m 62.5%	6.0 r/m 50.0%	4.7 r/m 39.1%	3.7 r/m 30.8%
0.125 Å eff. 300 kv. (peak) 1 mm. Cu	32.5 r/m 100%	29.0 r/m 89.2%	24.0 r/m 73.8%	20.3 r/m 62.4%	16.5 r/m 50.8%	12.7 r/m 39.1%	10.3 r/m 31.7%
0.100 Å eff. 300 kv. (peak) 2 mm. Cu	23.5 r/m 100%	21.0 r/m 89.3%	17.0 r/m 72.3%	14.7 r/m 62.5%	12.3 r/m 52.7%	9.7 r/m 41.3%	7.7 r/m 32.8%
0.075 Å eff. 300 kv. (peak) 4 mm. Cu	13.0 r/m 100%	11.3 r/m 87.0%	9.0 r/m 69.2%	8.0 r/m 61.5%	7.0 r/m 53.8%	5.7 r/m 43.8%	4.3 r/m 33.1%

results in a gain in the percentage depth intensity of only 2.7 per cent. These figures should not be interpreted as evidence that hardening the quality of radiation necessarily has very little influence upon the percentage depth dose, because that observation holds true only so long as improvements in the quality of the beam are made by the addition of relatively heavy filtration. In Tables II-IV it will be noted that the improvement in the relative intensity at a depth is proportionally greater

centage depth intensity of independently varying the voltage and the filtration, we were naturally interested in the effectiveness of various combinations of the two. A number of combinations had been employed so that it was an easy matter to compare the relative depth intensities as the effective wave length of the radiation was reduced in steps of 0.025 Å. Table XI shows such a comparison of depth intensities for seven different wave lengths varying from 0.225 to 0.075 Å. From a study of

Table IX it will again be noted that the harder radiation shows a relatively lower intensity within the superficial layers and a relatively higher intensity as the greater depths are reached. These differences are also indicated by the curves in Figure 5. A study of the data presented in Tables I-

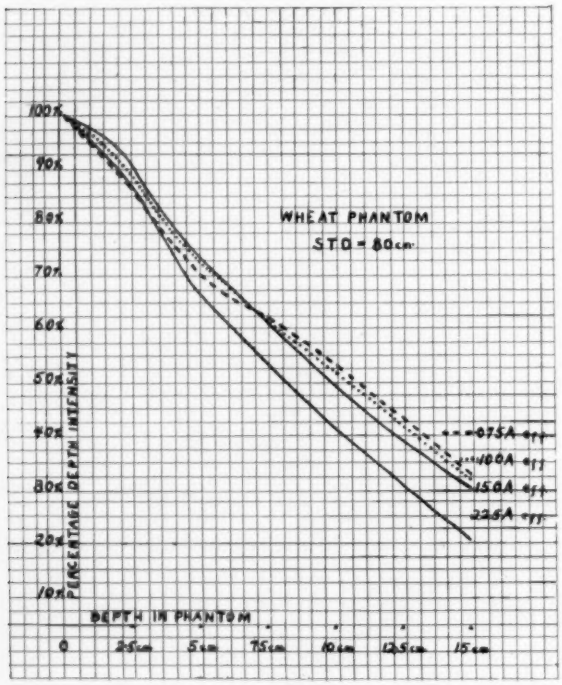

Fig. 5. Shows the absorption curves as determined in the wheat phantom for increasingly harder roentgen rays.

IX as well as the curves shown in Figures 1 and 5 has convinced us that conclusions based upon a study of the "percentage depth dose" at any single point may be rather misleading. While the differences in the percentage depth intensity at any single point may show little variation with differing qualities of radiation, it is evident that there may be significant differences in the distribution of radiation energy at varying depths when the curves are considered as a whole. In this connection we have repeatedly noted that there is an appreciable decrease in the proportion of scattered radiation on the surface of the medium as the thickness of the filter is increased. However, since we have been primarily concerned with intensities at a depth, we have made no attempt to include in this report a study of the relative quantities of radiation scattered back to the surface when different qualities of radiation are employed.

DISCUSSION

At the present time there is some question as to how high the voltage must be in order to realize the advantages claimed for "supervoltage" roentgen rays. Recent improvements in tube design have made equipment of 300,000 and 400,000 volts capacity as trustworthy and almost as practical to operate as the most modern types of 200 kv. apparatus. Since December, 1934, we have been operating "deep therapy" equipment at 300,000 volts, using a filter of 2 to 5 mm. of copper and a skin-target distance of 80 or 100 cm. Clinically, we have been impressed by the fact that normal tissues tolerate larger quantities of the harder radiation, and that immediate tumor regression is better than we have seen with the smaller dosages employed at lower voltages. On the other hand, we know that few phases of medicine have developed more rapidly than radiology, and this rapid growth makes it difficult to evaluate the modern trends in radiation therapy. Early in the course of their development it became evident that very high voltages have a somewhat limited usefulness and should not be employed for the treatment of all types of cancer. Although a great deal of discussion has arisen as to the relative merits of different voltages and different filters, there is probably little reason to expect that a single quality of radiation will ever be designated as the most desirable for all types of roentgen therapy. The effectiveness of the soft radiation of unfiltered low voltage roentgen rays in the treatment of skin cancer is evidently due to the fact that most of the energy is absorbed throughout the superficial layers of tissue. On the other hand, the treatment of deep-seated tumors probably requires harder, more penetrating rays

that will scatter less rapidly and deliver a greater proportion of their energy into the volume of the deeper lying structures.

We consider the resistance that a 10 cm. thickness of tissue offers to the passage of roentgen rays as only partially responsible for the decrease in the intensity of the radiation at that depth; a sizable proportion of this loss is simply due to the fact that the lesion is 10 cm. farther away from the target than is the intervening skin. That proportion of the loss of intensity which is due to this factor (increasing distance) can be made relatively small by ploying a target-to-skin distance that is long in comparison to the skin-to-tumor distance. It is also recognized that the quantity of radiation being absorbed within any one unit of the volume depends not only upon the rays that penetrate to that particular area but also upon the softer rays scattered into that region from adjacent volumes of irradiated tissue. While the percentage depth dose can thus be improved by the use of larger portals and a longer skin-target distance, it is generally agreed that the "hardness" or the penetrating power of roentgen rays is fundamentally determined by their wave lengths, which, in turn, are primarily determined by the voltage that is applied to the roentgen tube. In fact, Schmitz and others have suggested that eventually we will recognize an optimum wave length of roentgen rays to employ for the treatment of lesions at each particular depth. While in most instances the available equipment does not permit a choice over a very wide range of radiation qualities, there is a growing conviction that the relatively harder roentgen rays that can be obtained by heavier filtration at ordinary voltages will appreciably improve the results of deep therapy. Mattick, and Merritt and Rathbone have recently pointed out that this improvement is partly due to the fact that the skin and subcutaneous tissues tolerate relatively large quantities of the harder, heavily filtered roentgen rays before showing the same degree of reaction that limits treatment by softer radiation to a much lower total skin dose. In addition to this quantitative factor we must also keep in mind the possibility that harder radiation shows a greater selective or biologically differentiating action; but as Murphy and others have suggested, only a longer time for observation of cases will answer that particular question.

SUMMARY

In general agreement with previously reported studies, we have found little increase in the percentage depth intensity as the effective wave length is decreased by the use of heavier copper filters at voltages between 150 and 300 kv. (peak). With each increase in voltage, one can employ additional filter to advantage; but evidently we cannot materially improve the percentage depth dose by increasing the amount of copper filter over and above a certain "optimum" thickness for each particular voltage. At least this rule holds true as far as the percentage depth intensity at a depth of 10 cm. is concerned. In view of this fact, whenever it seems desirable to decrease the intensity of an available beam of radiation there is some reason to favor the use of longer skin-target distances rather than additional thicknesses of copper filter. On the other hand, from a study of their relative intensities at different depths within the phantom, we know that varying qualities of radiation show differences in the distribution of their energy which may not be apparent when we merely compare their relative intensities at a depth of 10 cm. It is evident that from a physical standpoint, the problem is a complicated one. Moreover, Taylor and Tucker have pointed out the inadequacy of the percentage depth dose as a means of evaluating the effectiveness of varying qualities of radiation and they have suggested it would be unwise to attempt to determine the most effective combination of physical factors for deep roentgen therapy upon the basis of physical measurements alone.

It is not the purpose of this report to at-

tempt an evaluation of either the physical or the clinical data that have been presented in the past. We know there are advantages to be gained by heavier filtration, which are beyond the scope of this paper to discuss, and at the present time we are convinced that an ultimate decision as to the most effective factors to employ in deep therapy must be determined by clinical as well as physical evaluations of the relative merits of heavier filtration, higher voltages and longer skin-target distances.

CONCLUSIONS

1. Conclusions based upon a study of the "percentage depth dose" at 10 cm. (or any other single point) may not provide a reliable means of evaluating the relative importance of the physical factors which determine the effectiveness of radiation at a depth.

2. Such differences as do exist become more evident when the relative depth intensities of varying qualities of radiation are studied at several depths within the phantom or when the comparison is based upon their "absorption curves" as a whole.

3. It is agreed that any attempt to determine the most effective combination of physical factors for deep roentgen therapy must be based upon clinical as well as physical evaluations of the relative merits of heavier filters, higher voltages and longer skin-target distances.

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RADIOLOGICAL APPLICATIONS OF THE GEIGER-MÜLLER COUNTER*

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NEW YORK CITY

IN RADIOLOGY we are from time to time faced with the problem of detecting rays of minute intensity, as in the measurement of stray radiation and in the search for lost radium. Until recently, the conventional type electrometer has been the principal device used for this purpose. However, that instrument has certain limitations, such as insufficient sensitivity, time-consuming operation, and lack of directional effect. To overcome these drawbacks, we designed and constructed more than a year ago a device of the Geiger-Müller counter type. More recently there has been reported in the radiological literature the development of somewhat similar type instruments by other workers such as Locher and Weatherwax,[1] and others.[2,3]

In this paper we shall limit ourselves to a description of the fundamentals of the apparatus and give more consideration to the measurements we have made with the instruments and their applications.

The heart of the instrument is the tube counter invented by Geiger and Müller[4] in 1928. The Geiger-Müller tube may be considered a special type of ionization chamber or spark gap in which the applied voltage across the electrodes is just below the corona point. Due to this high degree of electrical instability a single ionizing ray or particle is sufficient to cause a discharge through the tube by its trigger-like action whereby the minute amount of radiant energy releases much larger energies.

DESCRIPTION OF APPARATUS

The construction of the apparatus is shown diagrammatically in Figure 1. The Geiger-Müller tube consists essentially of a sealed glass tube in which is mounted a metal cylinder with a fine wire stretched along its axis. The cylinder is connected to the negative pole of the voltage source which may be a battery or, as in our apparatus, rectified, filtered alternating current. The center wire is connected to ground through a high resistance. In order to avoid excessively high voltages the pressure of the gas, argon, is suitably reduced (2 to 10 cm. Hg). When a gamma ray or roentgen ray passes through the counter it causes a discharge due to the secondary emission of ions from the wall of the electrode and resultant ionization of the gas. As the discharge current passes through the tube the potential across electrodes falls due to the voltage drop in the resistors and the discharge is quenched bringing the Geiger-Müller tube back to its original condition. These pulse-like changes in voltage across the tube are detected by means of a resistor condenser arrangement. For a certain range of potential difference between the cylinder and the central wire the number of pulses is proportional to the quantity of radiation passing through the tube. Those pulses are rather small and must be amplified in order to be readily detected, by ear phones, loud speaker, or by electrical recording devices.

The complete circuit used in our latest apparatus is shown in Figure 2. In this instrument the first amplifying tube and all the other parts shown within the dotted enclosure are mounted with the Geiger-Müller tube in a small compartment and connected by means of a 25-foot cable to the rest of the apparatus, as illustrated in Figure 3. In the earlier model the Geiger-Müller tube is in a separate holder and there is a rather low limit to the length of

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the connecting cable due to its capacity, which tends to decrease the impulse before it is amplified by the first tube.

DESCRIPTION OF GEIGER-MÜLLER TUBES USED

The Geiger-Müller tubes were designed and constructed to fulfill the following requirements: Since they are to be almost completely surrounded with lead to produce a directional effect, it is desirable to have them small and compact to avoid excessive weight. They should have a small background count; by the background is understood the natural count due to cosmic radiation and the inherent presence of minute quantities of radioactive substance in the building materials and earth. It is important to have the counter tubes so constructed that they will function when a comparatively low voltage is applied between the metal cylinder and the central wire. Above all, they should have a long life and yield stable operation over a period of several years.

In order to construct a tube with a low background count small metal cylinders made of aluminum were carefully machined and then polished first with powdered carborundum and finally finished with jeweler's rouge. A 4-mil tungsten wire served as the central electrode. It was carefully cleaned with alcohol before being put in place. No further treatment of the wire is necessary. Tubes of this type were found to have a background, or natural count, as low as 5 per minute.

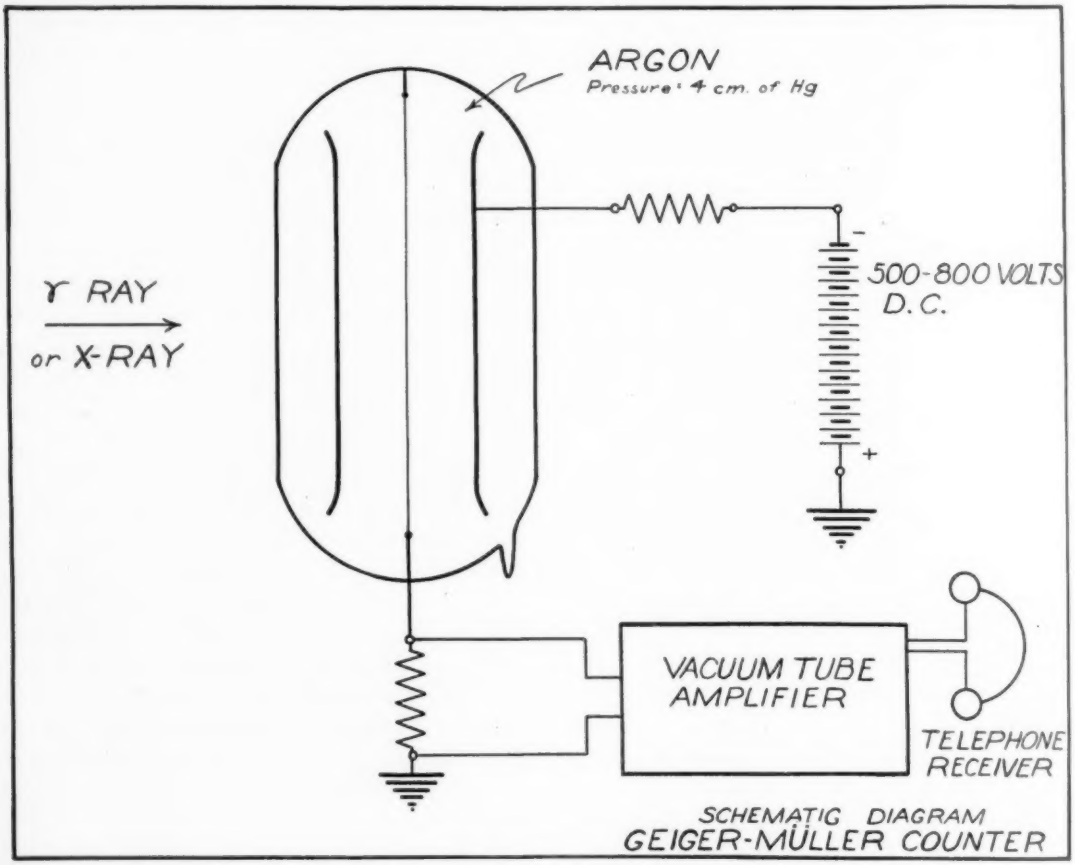

FIG. 1. Schematic diagram of Geiger-Müller counter.

The low voltage operation was obtained by carefully removing all traces of water vapor by continual baking and pumping, and then filled with argon, through a liquid air trap, to a pressure of about 4 cm. of

mercury. Tubes thus made and treated were found to operate satisfactorily on a potential of about 500 volts.

Long life and stable operating tubes were made by completely sealing them in glass. Instead of wax joints all seals were made by fusing the glass directly to tungsten rods. This also has the important advantage of permitting one to bake out the tubes at a rather high temperature, which is very effective in removing water vapor. It was deemed advisable to have tubes with different sensitivities. This was accomplished by employing metal cylinders of different lengths. Some tubes were made with cylinders 4.4 cm. in length while others were only half this length. The latter gives a sensitivity of about one-half of the former.

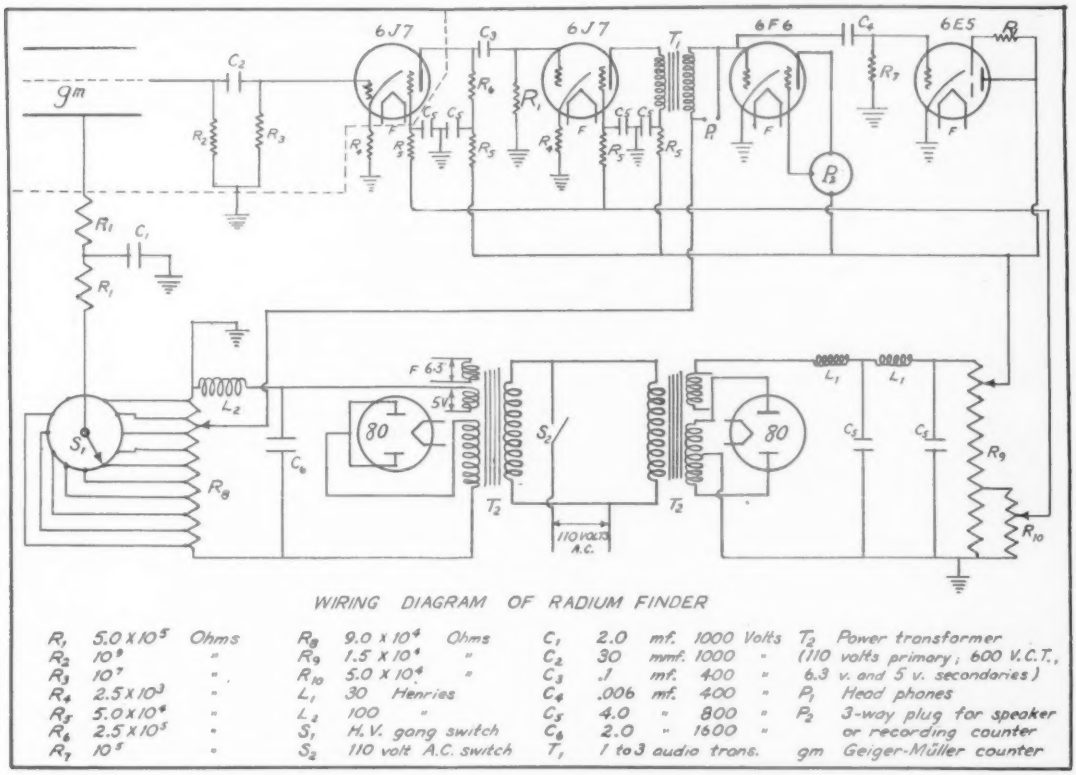
6J7
6J7
6F6
6E5
gm
80
80
110 VOLTS A.C.
WIRING DIAGRAM OF RADIUM FINDER
R1 5.0 X 10^5 Ohms
R2 10^9 "
R3 10^7 "
R4 2.5 X 10^3 "
R5 5.0 X 10^4 "
R6 2.5 X 10^5 "
R7 10^5 "
R8 9.0 X 10^4 Ohms
R9 1.5 X 10^4 "
R10 5.0 X 10^4 "
L1 30 Henries
L2 100 "
S1 H.V. gang switch
S2 110 volt A.C. switch
C1 2.0 mf. 1000 Volts
C2 30 mmf. 1000 "
C3 .1 mf. 400 "
C4 .006 mf. 400 "
C5 4.0 " 800 "
C6 2.0 " 1600 "
T1 1 to 3 audio trans.
T2 Power transformer (110 volts primary; 600 V.C.T., 6.3 v. and 5 v. secondaries)
P1 Head phones
P2 3-way plug for speaker or recording counter
gm Geiger-Müller counter

Fig. 2. Wiring diagram of radium finder. The same circuit is used when the apparatus is employed for stray radiation measurements.

meters from a 2 mg. radium needle suspended in air. The counting rate, that is the net number of counts per minute, was determined for the different angles and plotted in percentage of the sensitivity obtained in the forward direction. It will be noted that the number of counts remains nearly constant within 15° to either side of the axis of the tube and then decreases rapidly to about 50 per cent as the lead shielding becomes more and more effective. This effect is particularly an advantage in the search for lost radium, as the

USE OF THE APPARATUS AS A RADIUM FINDER

One of the outstanding features of the Geiger-Müller tube as a radium finder is the directional effect so easily obtained. This was done in our case by simply placing the tube in the center of a lead cylinder about 12 cm. in length, leaving 2 cm. of lead all around the tube except at the ends. The effectiveness of this arrangement is clearly illustrated in Figure 4. In this chart is indicated the variation in sensitivity with direction plotted on polar coördinates.

The Geiger-Müller tube was placed 2

direction is immediately indicated by the greater response of the counter. The range of this particular counter is about 15 feet for 1 mg. That is, within that distance the counts will be at least twice that of the background and can therefore easily be detected. For greater radioactive quantities, the range obviously is larger. Using the inverse square law we have that the range for this counter, in general, is equal to 15 times the square root of the quantity in milligrams or millicuries; 25 mg., therefore, can be detected at $15 \times \sqrt{25} = 75$ ft. This, of course, assumes the absence of any intermediate absorbing object.

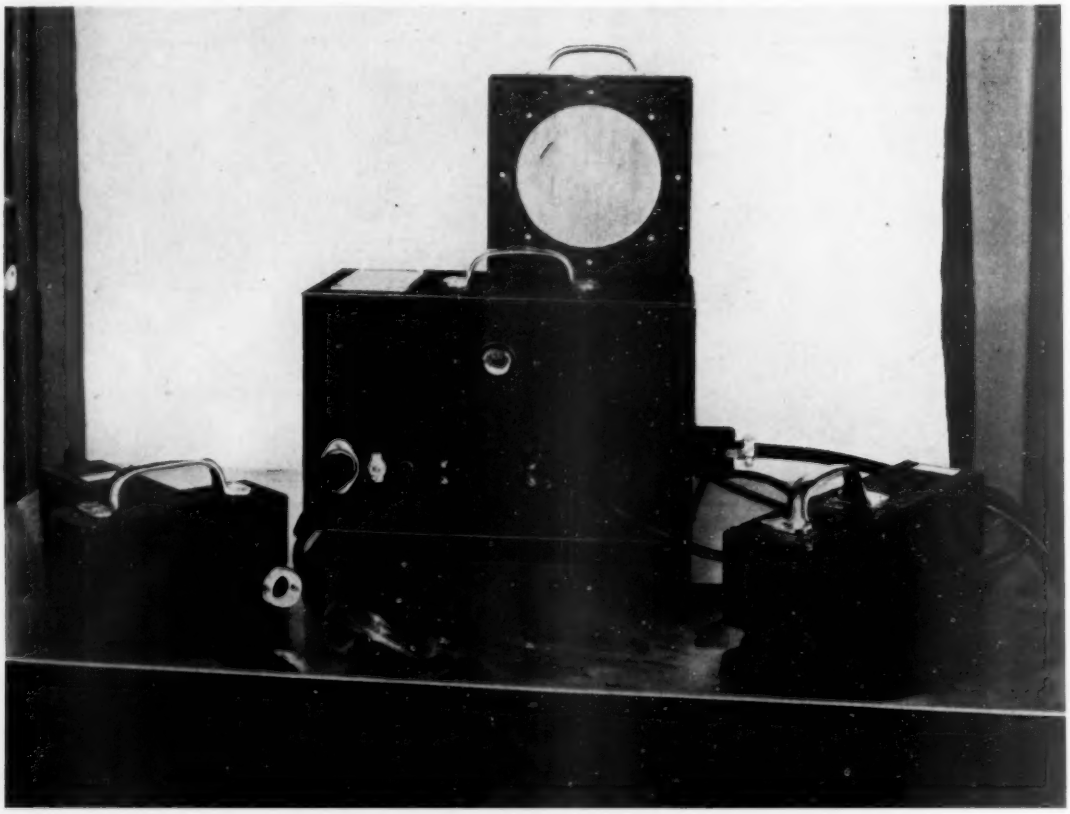

FIG. 3. Photograph of apparatus.

Both instruments have already on several occasions served their purpose as radium finders. In the Cancer Division of the Department of Hospitals we have a total of 10 grams of radium, of which 3 grams are distributed in the form of tubes and needles among the various institutions. As might be expected, losses have occurred from time to time, but since we have used these instruments, the misplaced radium or radon has always been recovered. Several needles have been located in the ashes of incinerators and very recently we found 30 mg. of radium in a drain pipe of one of the city hospitals after a search of less than an hour.

Our interest in recovering misplaced radioactive materials is not solely to avoid the economic loss. There is always the possibility of a person unknowingly carrying the radium or radon in his clothing with resultant dangerous effects. By means of this instrument we found, for instance, that the vest of one of the radium technicians was radioactive due to contamination caused by the breakage of a radon tube.

USE OF THE APPARATUS FOR STRAY RADIATION MEASUREMENTS

Both Geiger-Müller counters were designed primarily as radium finders. How-

ever, later tests indicated that their field of application could be extended to include stray radiation measurements.

A series of calibration tests was made with various types of counter tubes to determine their sensitivity to different qualities of roentgen rays. It was necessary in these measurements to use a long focal distance and reduce the active cross-section of the counter tube by means of diaphragms to cut down the number of counts per minute. There is always an upper limit to the counting rate above which the response is no longer proportional to the intensity of radiation as the apparatus has insufficient time to recover between impulses. All the measurements were made well below this limit, which in our case was determined by the time lag of the relays of the electrical recording device.

In Figure 5 is shown the arrangement used in the calibration. The roentgens per minute were measured at 65 cm. focal distance by means of the Taylor type of standard ionization chamber. The corresponding intensities were determined for the 930 cm. distance of the Geiger-Müller counter, using the inverse square law and making correction for air absorption. The correction factors were obtained by comparative measurements at 65 cm. and 930 cm., using a thimble type ionization chamber. Our experimental results thus obtained check closely with the air absorption coefficients published by Grebe and Nitzge[5] for shorter wave lengths.

The Geiger-Müller tube was mounted in a holder constructed especially for roentgen-ray measurements. The tube axis was arranged perpendicularly to the roentgen-

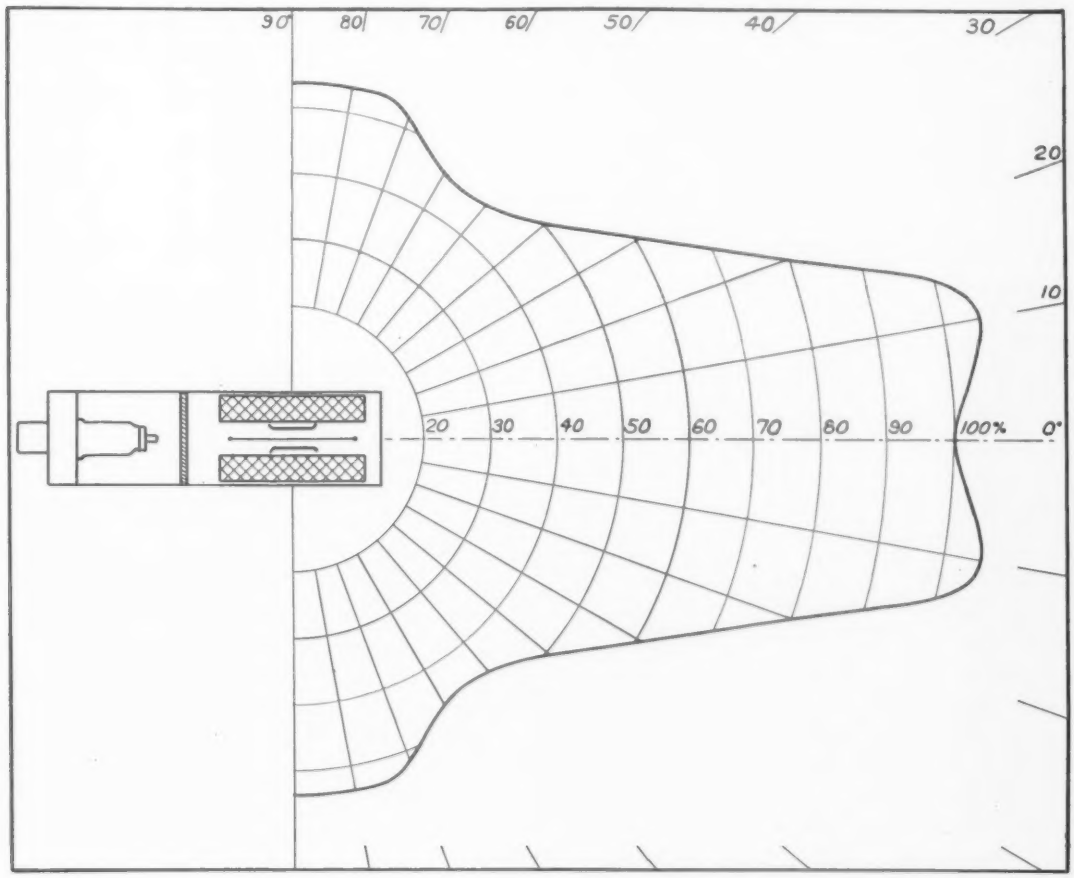

Fig. 4. Directional sensitivity of radium finder. The curve indicates the directional sensitivity in percentage of the response in the forward direction.

ray beam to obtain maximum response even for the smaller openings. A collimator tube was provided for the insertion of diaphragms of various sizes. The calibration of the counter was made for different wave lengths from 100 kv. unfiltered radiation to 200 kv. filtered through 2 mm. copper and 1 mm. aluminum.

value layers of copper. It will be noted that the shape of the curve is very similar to the calibration curves for thimble type chambers. The response of the counter remains nearly constant for the harder radiation. As the radiation becomes softer, the sensitivity decreases rather rapidly, that is, it requires a greater quantity of radiation to

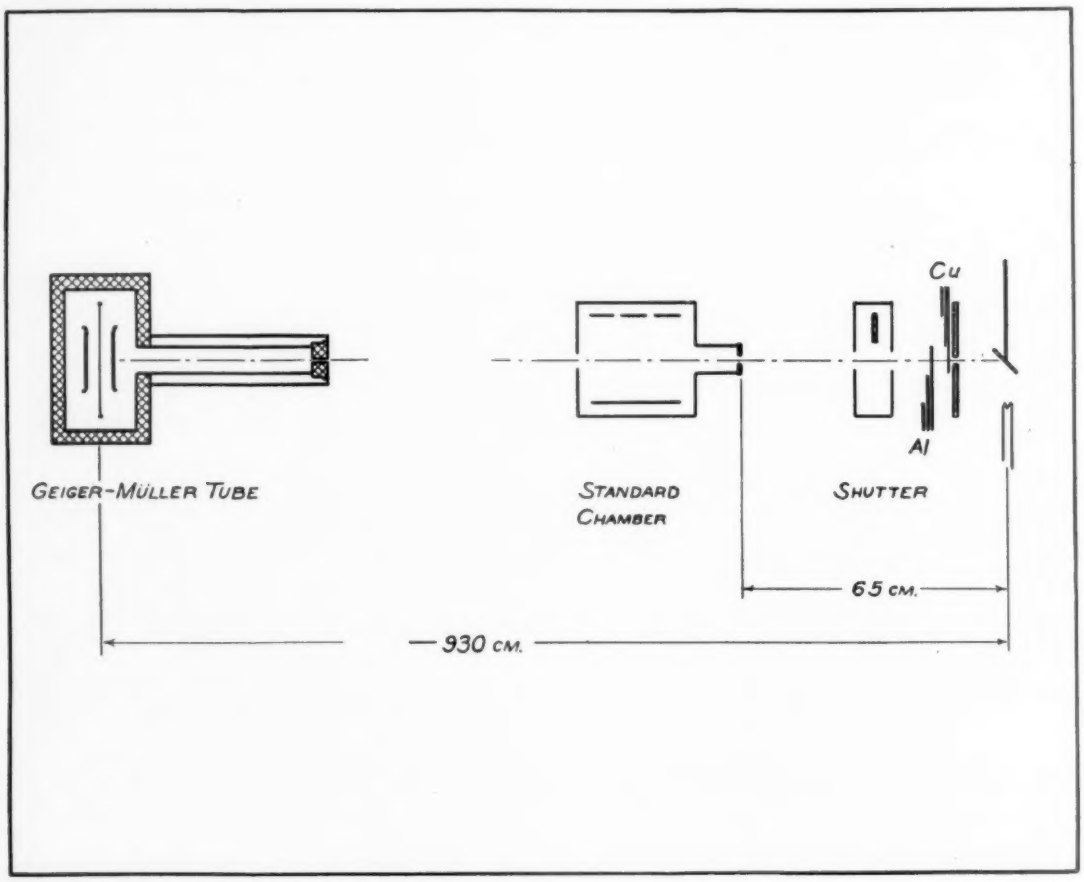

FIG. 5. Arrangement used in the calibration of the Geiger-Müller counter. The actual distance between the Geiger-Müller tube and the standard chamber is much greater than indicated on the drawing.

To minimize errors due to statistical fluctuations the average count of several five-minute periods was determined for each ray quality. The results thus obtained are shown in Figure 6. In this chart is plotted the sensitivity of the counter with respect to ray quality. The sensitivity is expressed in terms of milliroentgens per count, 1 milliroentgen being 1/1000 part of a roentgen. The quality is given in half-

produce one count. This decrease in sensitivity may be explained by the absorption of the longer wave lengths in the glass and in the aluminum cylinder of the Geiger-Müller tube.

In order to secure more independence of the wave length, we constructed and tested four different types of counters with cylinders of thin carbon in place of aluminum. The results of our measurements so far

have not been conclusive due to difficulties in obtaining a low background apparently caused by spontaneous discharges.

It will be noted that the aluminum counter requires about 0.07 milliroentgen per count for the harder radiation. This means that 1 milliroentgen will cause about 14 counts. As the calibration of the counter was made with a 1 mm. diaphragm, 100 1 milliroentgen per minute is permissible. As this intensity is at least one hundred times the minimum detectable with the counter, a great factor of safety is provided in the measurements.

The apparatus may be so constructed that it measures the stray radiation from all sides or from just one direction. The latter arrangement is used in our counter

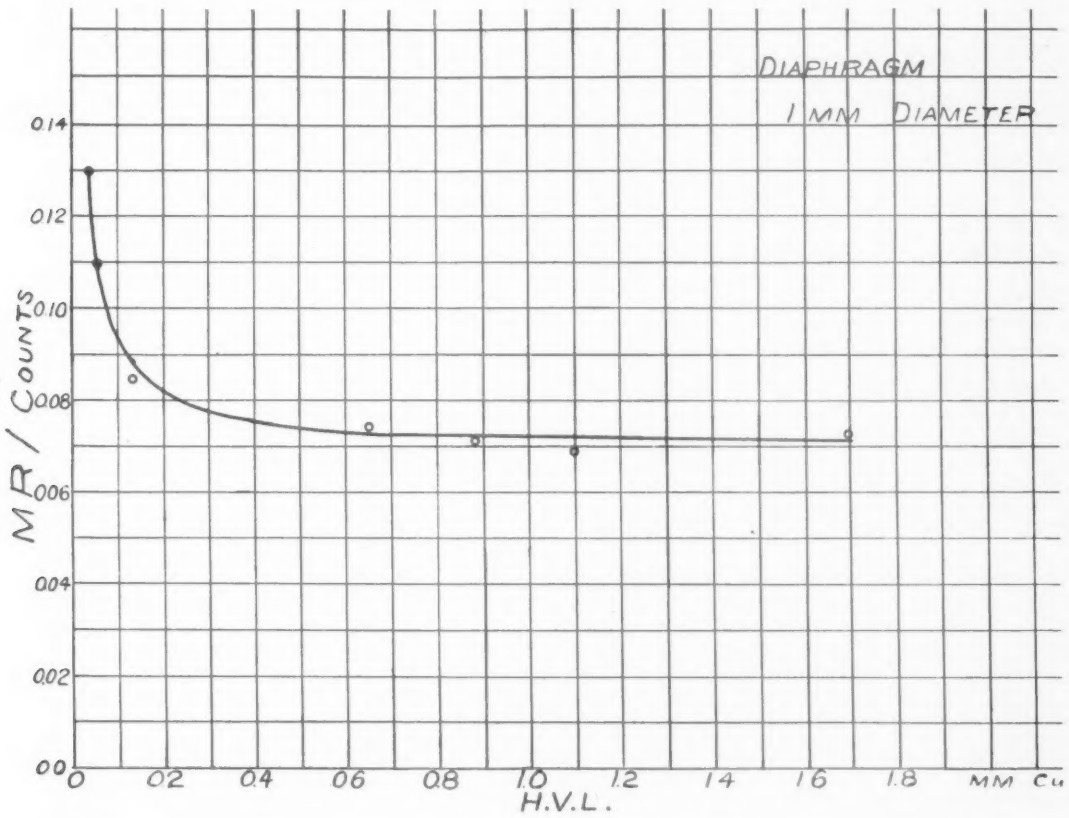

Fig. 6. Calibration curve of the Geiger-Müller counter.

times this sensitivity could readily be obtained by increasing the size of the diaphragm. With a larger diaphragm, it is therefore possible to detect, without any difficulty, intensities as low as 1/100 part of a milliroentgen, that is, 1/100,000 part of a roentgen or 10 microroentgens.

This exceedingly high sensitivity makes the instrument particularly suitable for stray radiation measurements. If we consider 1.5 roentgens the weekly tolerance dose, a maximum stray radiation of about

holder which makes it a valuable tool in the study of roentgen-ray protection. By merely pointing the holder in various directions it is possible, for instance, to determine in a given installation how much of the stray radiation is due to scattering from the ceiling and how much is caused by insufficient protection of the walls. Another advantage of the instrument is the ease with which the sensitivity can be changed by using different-sized diaphragms or Geiger-Müller tubes.

CONCLUSIONS

It should be emphasized that most of the experimental work here reported has been carried out with apparatus originally designed for portable use rather than for quantitative measurements. Yet the consistency of the obtained results in addition to the portability and exceedingly high sensitivity of the apparatus indicates that the Geiger-Müller counter has distinct advantages in the measurement of stray radiation. Furthermore, gamma- or roentgen-ray shielding with resultant directional effect may be obtained, when wanted, without adding such excessive weight as would be required to shield ionometric instruments.

Further investigations are now being carried out with the aim of constructing counters with less variation in sensitivity with wave length. However, even in the present form of the counter this variation is insignificant when compared, for instance, to the great wave length dependence of films which are so widely used in checking protection.

We wish to acknowledge the valued aid rendered by I. Hanson Blatz with the experimental work and by O. Telfair Smith with the preparations of the diagrams.

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EDITORIAL

THE DANGERS OF ROENTGENOSCOPY: SUMMARY AND RECOMMENDATIONS

THE importance of roentgenoscopy as a diagnostic procedure cannot be overemphasized, particularly in those instances in which an exact knowledge not only of structural deformities but even of functional changes is necessary, for example, in the diagnosis of diseases of the gastrointestinal tract, in the study of the heart and lungs, and in the treatment of fractures. In fact, roentgenologic methods of diagnosis are so important that no investigation of a patient is considered complete without roentgenologic examinations, which generally include roentgenoscopy. These studies often are carried out by a general practitioner or surgeon in his office because of lack of facilities for expert study nearby or because the physician sees no need to refer the patient to a roentgenologist. In many localities it is cheaper and more convenient "to have some pictures made" in "an x-ray laboratory" operated by a layman than it is to have the appropriate examinations made by a roentgenologist.

From data available from the Bureau of Census and from manufacturers, it has been impossible for me to find out the number of roentgen machines in use in this country. But various estimates which have been given to me indicate that perhaps 2 to 5 per cent of all physicians in this country have roentgenologic equipment of some kind in their offices. When one considers the number of diplomates of the American Board of Radiology in contrast to the number of physicians and others who "do a little x-ray work" one can estimate roughly the magnitude of the risk of injury that those in this latter group run from casual and nonexpert roentgenologic procedures. With such a great number of roentgen machines in use, one wonders whether injuries by roentgen rays will not be even more common in the immediate future than they were in the tragic days of the pioneers in roentgenology.

It is well known that the majority of physicians who suffered injuries which oftentimes led to their death sustained these injuries in the course of roentgenoscopy. The story of the tortures endured by physicians who had extensive roentgen burns has been often and well told. One needs but to read the masterpiece by Brown, "American Martyrs to Science through the Roentgen Rays," to appreciate the tragedy likely to follow the indiscriminate, careless, indifferent or even ignorant use of the roentgenoscope.

Published reports have indicated that the causes of injury to the early workers in the order of frequency were: roentgenoscopy, roentgen therapy and roentgenography. The same causes of injury hold true at the present time, as was demonstrated in a recent review which I made of the causes of the roentgen injury sustained by fifty-five physicians. Stevenson and Leddy, in their study on the dangers of reducing fractures under the roentgenoscope, demonstrated that the greatest danger in roentgenoscopy was from the use of unprotected roentgen rays. They also emphasized that the danger was greatest among roentgenoscopists who had not received special training.

The necessity for mechanical and physical protection against roentgen rays has been recognized ever since these rays were discovered; it has been recognized officially since the organization of the British Safety Committee in 1921. For years the International Safety Committee has made

periodic recommendations about protection in roentgenology. But several of these recommendations are not clear cut, definite and specific, particularly as regards physicians who do not have any special knowledge of the physical or the technical phases of roentgenologic diagnosis. Furthermore, many physicians who "do a little x-ray work" have never heard of this Committee or of its recommendations. Then, too, some of the recommendations of this Committee are antiquated, particularly those which refer to autoprotecting roentgen tubes, which are commonly used. The recommendations are not up-to-date regarding modern diaphragms, films and screens.

Because the American literature of the past ten years contains shockingly little about protection against radiation in roentgenoscopic procedures, I am fearful about injuries in the future and hope that they may be minimized by the work of suitable committees.

Fortunately, the limit of safety, or the so-called tolerance dose, on which the recommendations for protection are based, is extremely safe. This was proved by Cilley, Leddy and Kirklin[3–8,11] and by Barclay,[1] whose reports have been published in this JOURNAL. These authors said that the tolerance dose is very safe and they showed that multiples of the "tolerance dose" can be sustained without any apparent injury.

From the standpoint of mechanical protection, the manufacturers of roentgen tubes and apparatus deserve great credit for their activities in protecting the roentgenologist. All roentgenologists know that many safety devices were originated and developed by manufacturers and not by roentgenologists.

Since inexpensive and accurate dosimeters are available everywhere, there is no excuse for a roentgenologist not knowing both the limit of safety of roentgenography when performed with his own apparatus and the doses to which he may be exposed in the course of roentgenoscopic examinations. Turnbull pointed out the uncertainty with which diagnostic procedures are often carried out in this country. He described one method for determining the limit of safety and gave some illustrative values.

In our studies of the safety of roentgenoscopy as carried out by the roentgenologists of The Mayo Clinic, in contrast with the dangers of the same procedure as conducted by the ordinary physician, we have shown that the experience and training of roentgenologists are just as important as mechanical protection. Lead rubber gloves, lead rubber aprons and protective devices around the roentgen machine are often so bulky and inconvenient to use that they are discarded by the physician who is not a roentgenologist. On the other hand, Cilley, Leddy and Kirklin[4–8,11] showed that such devices are unnecessary for the protection of the skilled worker. The roentgenoscopists at The Clinic use no protection for their hands or body, but are not injured by roentgen rays because they use a carefully worked-out, expert technique in their examinations. They adapt their eyes fully to darkness; they work rapidly; they use a small beam, and they keep the examining hand out of the field illuminated on the screen. But, most of all, they use a carefully developed technique by which the gastrointestinal tract is investigated in the shortest possible time and with a minimum of exposure during the diagnostic procedure.

In the five years since the report by Cilley, Leddy and Kirklin[4–8,11] was prepared the roentgenoscopists at The Clinic have continued to use the same procedures, and in spite of much additional "absorption" of radiation by these men, they still show absolutely no evidence of any injury. From the experience of this group, therefore, I feel that skill and technique in examination are of as great importance in protecting the roentgenologist as are purely mechanical devices.

But the unskilled physician who carries out roentgenoscopic examinations only

casually and, therefore, not expertly, should always use every available method of mechanical protection.

RECOMMENDATIONS

From our studies at The Clinic I think that the dangers of roentgenoscopy could be minimized if each roentgenologist determined for himself, with his own roentgenoscope, the time required to produce an erythema dose—in terms of roentgens.

The method of determining the limits of safety as outlined by Turnbull and Leddy could be used to this end and modified to suit variations in roentgenoscopic screens and films which elsewhere undoubtedly differ from those used by them.

Acting on the suggestion made in Stevenson's paper, I should recommend that the roentgenoscopic reduction of fractures be abandoned entirely and that some method of producing roentgenograms rapidly in the operating room should be adopted in its place.

Since the specified lead rubber gloves and aprons are not used by many roentgenologists and others on account of their bulkiness and clumsiness, I would suggest that some light protecting material, such as that recommended by Kirklin, be adopted and worn to protect against doses of roentgen rays which, in the case of the nonexpert roentgenoscopist, are a potential source of great danger.

Even though the "tolerance dose" seems excessive and is not well grounded clinically, I feel, nevertheless, that it should be maintained. To establish the exact value of the "tolerance dose" would be purely a matter of academic interest. Inaccurate as it may be, the tolerance dose is safe, and protective measures calculated on the basis of this dose are safe. To abandon it or to change it would necessitate expensive and extensive changes in roentgen apparatus throughout the world, a step which would be risky and senseless.

In my study on the causes of roentgen injuries among physicians it was brought out that many of them did not realize that the changes in the skin of their hands were due to roentgen rays, and they exaggerated the already existing injury by their treatment. Therefore, it is suggested that any injury to a roentgenologist's hands or fingers should not be treated with ultraviolet light, roentgen rays, or radium, but that some other treatment be used.

Since Stevenson and Leddy have pointed out that the roentgenoscopic reduction of fractures is often performed by physicians who have never had any special roentgenologic training, and particularly by surgeons, general practitioners and hospital interns, I think that the dangers of roentgenoscopic reduction of fractures should be emphasized repeatedly to these physicians.

The most important protection with which any roentgenologist can surround himself is skill and a perfect technique of roentgenoscopic examination. Secondary to these is mechanical protection.

The recommendations of the Safety Committee should be published once a year, and should be more widely circulated in the nonroentgenologic literature which is read by those who "do a little x-ray work." One must distinguish clearly and emphatically the fact that the physician who "does a little x-ray work" has an entirely different risk from that of the expert roentgenologist. It is the physicians in the first group who *need* protection.

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Eugene T. Leddy

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. B. Peirce, University Hospital. Ann Arbor, Mich. Annual Meeting: Atlantic City, Sept. 20–23, 1938.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting, 1938: To be announced.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting, 1938: To be announced.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1938: To be announced.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY
Secretary, Dr. Howard H. Ashbury, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Special meetings may be called by the Chairman.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, E. N. Liljedahl, Los Angeles, Calif. Meets on the second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. North W. Shetter, 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

CONFERENCE OF EASTERN RADIOLOGISTS
Secretary, Dr. B. R. Young, Temple University Hospital, Philadelphia, Pa. Meets Philadelphia, Jan. 28 and 29, 1938.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. N. B. Newcomer, 306 Republic Bldg., Denver, Colo. Meets third Tuesday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Harold O. Brown, Tampa, Florida. Meetings held twice a year, May and November.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. S. G. Schenck, 115 Eastern Parkway, Brooklyn, N. Y. Meets at Kings County Med. Soc. Bldg. on third Thursday of each month from October to May, at 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. R. W. Lewis, 140 E. 54th St., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Two day annual meeting, May, 1938. Exact date and place to be decided.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. H. N. Mawhinney, Mercy Hospital. Two fall and two spring meetings—time and place designated by the president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

South Carolina X-Ray Society
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston.
Meets at time and place of South Carolina Medical Assn.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. M. H. Glover, 414 Hamilton Bldg., Wichita Falls, Texas. Meets Nov. 20, 1937, in Dallas, at Adolphus Hotel.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich. Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section on Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September 12, Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson, Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

OUTLINE OF AN UNDERGRADUATE COURSE OF INSTRUCTION IN RADIOLOGY

The teaching of radiology to undergraduates is still in the developmental period and medical faculties are confronted with the following questions.

(a) How many teaching hours should be allotted to radiology?

(b) Shall the teaching of radiology be spread over the four college years or crowded into one semester of a single year?

(c) Is radiology a circumscribed specialty or has it expanded into one of the fundamental branches of medicine of importance equal to the other major branches?

(d) Shall the teaching of radiology be entirely encompassed and absorbed by the several major pre-clinical and clinical branches of medicine or shall there be adequate time allotted also to the teaching of fundamental or "pure" radiology?

Discussion. (a) Medical teachers in general and radiologists in particular were long ago convinced that the old method (which still obtains in some medical schools) of allotting sixteen hours during one semester to cover the entire diagnostic and therapeutic field of radiology has been inadequate. When holidays, examination periods, etc., are deducted, the actual teaching amounted to twelve hours or less and the course of instruction degenerated into the mere cataloguing of the various applications of the subject as might be presented before a nonmedical audience.

(b) If the instruction is condensed into one year (usually the junior or senior year) as formerly, the student was not only unable to understand the subject as a fundamental medical science because of its complexity, but was also unable to grasp the full significance of its application to all of the pre-clinical and clinical branches of medicine. If, however, radiological construction is begun with anatomy in the freshman year and continued in relatively brief courses each year thereafter, the student will gradually build up a complete and sound conception of this branch of medical science.

(c) In the detection and study of disease processes, diagnostic roentgenology is attaining a position of importance comparable to that of pathology, with the added advantage that the roentgen method reveals the disease process in the *living*. Being the most important modality in the field of physical therapy, roentgen and radium therapy is assuming an importance approaching that of drug and serum therapy. From freshman anatomy to senior surgery and medicine, radiology is always in evidence as an aid and a guide. Thus radiology seems to measure up to the requirement of a major branch of medicine rather than a specialty.

(d) All radiologists are emphatically in accord with medical teachers in the conviction that the teaching of radiology should be largely clinical and carried out in connection with bedside instruction and ward rounds, as well as in the out-patient clinic, in clinical-pathological conferences and routine medical and surgical lectures and demonstrations. But there is an equally firm conviction among radiologists that a certain amount of instruction in "pure" radiology is necessary to lay a foundation and to prepare the students for an intelligent application of radiology to clinical medicine. Such instruction in "pure" radiology is sometimes incorrectly termed "detached" instruction in the sense that it is not given at the bedside or concerning a single specific patient. Radiologists, experienced in teaching, never "detach" their presentations from the clinical aspects of medicine. If, for example, mediastinal abnormalities are being discussed the full history and clinical details should accompany each roentgen film or lantern slide shown. If radiotherapy is under discussion, the clinical application to specific cases should be stressed and case histories presented.

General Deductions. Authorities on medical teaching have stated that training in

the specialties is and should be a function of graduate study. It therefore should not be the aim of an undergraduate radiologic course to make specialists, but simply to give sufficient instruction for the needs of the general practice of medicine.

Assuming the above reasoning to be sound, an attempt has been made during the past two years to carry out the appended schedule at the University of Cincinnati Medical School. Referring to this schedule, attention is called to the fact that the course is distributed over the four college years as follows:

Course 11b	Freshman year
Course 21a, Course 21b	Sophomore year
Course 31	Junior year
Course 100a to 103	Senior year

Attention is also called to the fact that the appended schedule covers only the courses offered by the radiologic staff and does not include the relatively greater amount of instruction in "clinical radiology" given daily in practically all of the various departments of college and hospital.

RADIOLOGY

11b. Radiologic Anatomy.—Th., 2:00–3:00.
Radiologic Staff
Eight hours devoted to demonstration of the normal anatomic relations of the organs of the chest and abdomen, as revealed by the X-ray.

21a. Radiologic Physiology.—Th., 1:30–2:30.
Radiologic Staff
Eight hours of fluoroscopic demonstrations given by the Department of Physiology in connection with its lectures and laboratory courses.

21b. Radiologic Pathology.—F., 2:00–3:00.
Radiologic Staff
Eight hours of bone pathology (and a comparison with the normal) as revealed by the X-ray.

31. Interpretation of X-Ray Films in Medical and Surgical Diagnosis.—*First semester*, Tu., 2:00–3:00; *second semester*, M., 2:00–3:00. One-half credit.
Radiologic Staff
Eight hours of demonstrations for each junior group.

Electives

100a. General Radiology.—M., 5:00–6:00.
Dr. Lange and Staff
Sixteen hours devoted either to a review of the subject for the general clinician or to group instruction in any special branch that may be selected by the students.
Sec. 1. Physics of the X-ray and Radium; Principles of Technique.
Sec. 2. X-ray Diagnosis as Applied to Special Branches of Medicine.
Sec. 3. Biologic Effects of X-ray and Radium.
Sec. 4. Radiotherapy.

101. Clinical Radiology.—Daily clinics in the X-ray Laboratory.
Sec. 1. Interpretation and Discussion of X-ray Films.—9:00–12:00.
Sec. 2. Radio-therapy.—2:00–4:00.
Dr. Reineke and Resident Staff

102. Practical Radiology.—Opportunity is given advanced students and graduates in medicine to serve as assistants in radiographic and radio-therapeutic Work.
Dr. Lange and Staff

103. Radiologic Research.—By arrangement with the Head of the Department.

Sidney Lange

Professor of Radiology
University of Cincinnati

DR. CORSON HONORED

On the evening of October 21, 1937, the Georgia Medical Society honored one of its distinguished members, Dr. Eugene Rollin Corson, by presenting him with an illuminated testimonial for notable service in research work and for pioneering in the field of roentgenology. The occasion was a dinner given in Dr. Corson's honor at which more than sixty members of the medical profession gathered to pay tribute to him personally and to compliment him on his many accomplishments in medical research. His scientific attainments were reviewed by doctors who had been his personal friends for years and knew intimately of his researches. Dr. Corson was also presented a substantial gift by the Society. Dr. Corson began his work in roentgenology in 1896 and during these years he has contributed many original articles dealing with his researches in this field as well as in many other phases of medical investigation.

DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., M.S., 105 Rutledge Ave., Charleston, S. C.

A SURGICAL TABLE MODIFIED FOR ENCEPHALOGRAPHY*

By Y. D. KOSKOFF, M.D.
PITTSBURGH, PENNSYLVANIA

THE value of encephalography as a diagnostic and therapeutic procedure has stimulated interest in techniques and devices designed to lessen reactions and reduce hazards. Modifications of the type of gas used[1] and of the method of injection[2,3,4,5] have appeared. Suitable chairs[6,7,8,9] have been devised which permit both gas injection and roentgenography without moving the patient. This valuable feature has served to reduce the patient's distress and is, in addition, of great convenience to the operator. To secure the combined advantages of a special chair and a standard operating table† the

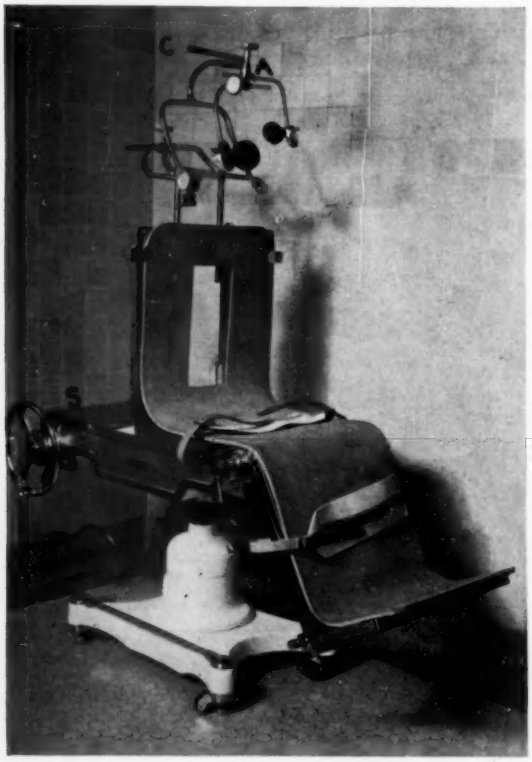

FIG. 1. Photograph of the table showing the maximum opening of the back; the metal shelf, *S*; the modified ganglion head rest with joints at *A* and *B* and handle at *C*.

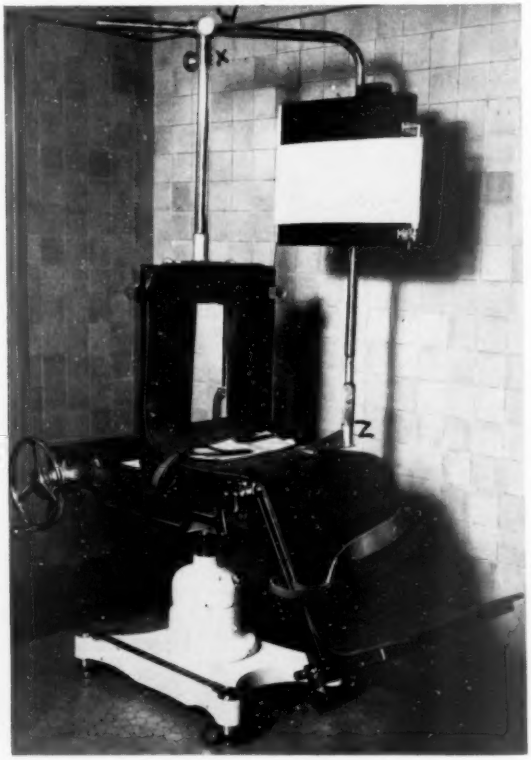

FIG. 2. View of table showing the steel attachment carrying the Potter-Bucky diaphragm; the joints at *W* and *X*, and the metal sleeve at *Z*.

† I wish to express my indebtedness to Mr. R. L. Jewell, Chief Engineer of the American Sterilizer Company, manufacturers of this table, for his suggestions and cooperation, and also to Dr. M. F. Goldsmith, Roentgenologist of the Montefiore Hospital, for his advice concerning the roentgenologic features of the table.

* From the Neurosurgical Service, Montefiore Hospital, Pittsburgh. Prepared with the aid of a grant from the Isaac Kaufmann Foundation.

following modification of the surgical table has been effected:

1. Two removable panels of different lengths were made in the back section of the table. By lifting out one or the other, or reversing their relative positions, an aperture size to suit the individual patient may be obtained. The maximum opening used for adults measures 15 by $7\frac{1}{4}$ inches. Standard shoulder, body and knee straps are used to secure the patient firmly against the opening. The back presents itself quite satisfactorily through the opening, permitting spinal pressure readings. It is protected from the metal by a thin rubber cushion.

2. A metal shelf, *S*, was made to cover the parallel projections of the base of the table when it is in the seat position. This overcomes the inconvenience of the projections by affording a sterile field upon which the operator may rest his hands during the air injection. It also provides a convenient place for the spinal fluid receptacle and other necessary equipment.

3. A ganglion head rest was provided with a hinged joint, *A*, a swivel joint, *B*, and a bakelite handle, *C*. By appropriate manipulation of the handle, the following movements of the head may be obtained: a "No" movement if joint *A* alone is loosened; a "Yes" movement if joint *B* alone is loosened; a clockwise or counterclockwise rotary movement if *A* and *B* are both loosened. Thus, changes in head position desired during the air injection may be smoothly performed. In addition, if the head rest is to be used for operations it affords enhanced flexibility for head adjustment.

4. A steel attachment, carrying a Potter-Bucky diaphragm, was designed to insert into the head piece grooves at the back of the table. The extension may be pushed forward or backward at joint *W* and rotated at joint *X*. The diaphragm may also be rotated on the extension as well as raised or lowered. Thus the appropriate position of the diaphragm may be obtained for anterior, posterior, and lateral views of the head. If desired, and we have found it quite expedient, a lateral and anterior and posterior view may be taken with the diaphragm in a single position by moderate turning of the patient's head. The remaining lateral film is secured by moving the diaphragm into position. Complete stability of the attachment is insured by the adjustable metal sleeve, *Z*, which rests on the table.

By these modifications economy of equipment is effected. The features of a special chair and those of a surgical table are combined. A desirable safety element is accomplished by bringing the procedure to the operating room where we feel that it best belongs. The construction of the table allows for smooth and quick changes of position affording an additional safety factor for the patient, should shock or other exigencies arise.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

BLAU, ABRAM; REIDER, NORMAN, and BENDER, MORRIS B. Extrapyramidal syndrome and encephalographic picture of progressive internal hydrocephalus in chronic hypoglycemia. *Ann. Int. Med.*, Dec., 1936, *10*, 910–920.

The authors report a case which was a neuropsychiatric problem and one which at intervals showed a marked hypoglycemia. This case was studied over a period of sixteen months of hospitalization during which time numerous tests and procedures were carried out. The patient was comatose when brought to Mount Sinai hospital; an intravenous injection of glucose was given, with no improvement; the hypoglycemic phase was therefore not considered for some time. He showed a progressive parkinsonian syndrome, transient attacks of polyneuritis, progressive bilateral nerve deafness, emotional and intellectual deterioration and progressive internal hydrocephalus. The fasting blood sugar values varied from 30 to 45 mg. per cent; after allowing for other reducing substances, the yeast fermentable sugar was estimated as low as 5 mg. per cent. Most of the attacks of coma occurred in the afternoon, even though the patient ate his lunch, and analyses of the blood showed that during some of the episodes of convulsions and coma, the blood sugar was relatively high, whereas at other times when the blood sugar was very low, no convulsions nor coma occurred. Moreover, glucose given by mouth, per rectum or subcutaneously was without result. Fever therapy was beneficial for several months—probably because of reducing the activity of the pancreas. Roentgen therapy directed to the pancreas was of no value. An exploratory laparotomy was performed, the viscera examined and sections were even taken from the liver and the pancreas but no abnormalities could be found, either grossly or by histological studies. Encephalography was performed twice, there being an interval of over eleven months between the studies. The second study showed an increase in the size of the ventricles. The authors suggest that the changes in the brain might have resulted from the repeated convulsions but they admit that the internal hydrocephalus might have been the result of a primary disease of the brain with a secondary hypoglycemia and convulsions. At least they believe that there is some relationship between disease of the periventricular nuclei and glucose metabolism.—*A. A. de Lorimier.*

NECK AND CHEST

TURNER, EDWARD L., and OPPENHEIMER, ALBERT. A common lesion of the cervical spine responsible for segmental neuritis. *Ann. Int. Med.*, Oct., 1936, *10*, 427–440.

A number of observers have noted definite relationship between a variety of neurological symptoms and spinal arthritis. In such cases there have been evidences of thickening of the periosteum of the vertebrae, thickenings of the connective tissue in the region of the joints and epidural exudate infiltrating the epidural areolar spaces. Schmorl has shown rupture of the nucleus pulposus with resulting collapse of the intervertebral disc and narrowing of the intervertebral space in cases where sciatic pains had been noted. Nachlas noticed that in several cases where arthritic changes were visualized in the lower cervical region, stabbing pains would be produced by acute hyperextension or lateral bending; these pains radiated to the scapular region and to the precordium. The authors are dealing with a survey of over 50 such cases and report the details of 5 of them as representative.

Most of this group were over fifty; 2 were only twenty-seven years of age. The common complaint was pain in some part of the shoulder arm, hand, back, precordium or neck; some claimed weakness or inability to carry out certain motions. In some the pains were severe and radiating; in others, merely paresthesias. Most of the cases had unilateral involvement, though in some the pains later extended to both sides, frequently manifesting some degree of atrophy on the side first involved. Roentgenographically various spinal changes were visualized but the consistent finding was narrowing of one or more of the intervertebral spaces in the cervical spine. By special technique a narrowing of the intervertebral foramina of the region was also visualized. Many of the cases showed lipping or

hypertrophic changes. Some showed displacements of one or more centra. In 3 of the 5 cases reported there was the history of remote injury. Most of the patients were relieved by having their heads propped forward (whereby the intervertebral foramina are widened). The middle and lower regions were most commonly involved (the 4th cervical supplies innervation over the top of the shoulder; the 5th, over the outer surface of the arm and between the shoulder; and elbow; the deltoid is supplied by branches from the 5th and 6th). Some of the patients were relieved by neck traction; some, by short wave diathermy; some, by roentgenotherapy. The use of soft rubber soles and heels is recommended.—*A. A. de Lorimier.*

JOHNSON, SYDNEY E. Congenital dilatation of the pulmonary arteries revealed by roentgenkymography. *Ann. Int. Med.*, Oct., 1936, *10*, 546–549.

The author emphasizes the diagnostic value of the kymograph. He reports a case of congenital heart disease where, roentgenographically, there was visualized a prominence in the region of the pulmonary conus with sharply defined masses projecting into both lung fields. The patient had been very healthy but an insurance examination prompted the roentgenogram because of a suspicion of his having tuberculosis. Roentgenographically, the differential possibilities included Hodgkin's disease or some other neoplasm and anomalies of the heart and great vessels. The patient was referred to the author for kymographic examination to determine whether the masses were vascular or solid tumor. This latter study showed definite expansile pulsations and established the diagnosis of congenital dilatation of the pulmonary arterial trunks and the probability of a patent ductus arteriosus.—*A. A. de Lorimier.*

DARLEY, WARD, and DOAN, CHARLES A. Primary pulmonary arteriosclerosis with polycythemia: associated with the chronic ingestion of abnormally large quantities of sodium chlorid (halophagia). *Am. J. M. Sc.*, May, 1936, *191*, 633–647.

A case of pulmonary arteriosclerosis with polycythemia was extensively studied by the authors. The patient came to operation and died and examination of the lungs and heart showed marked arteriosclerosis, a dilated pulmonary artery and a hypertrophied right heart. Theories as to etiology and the cases reported in the literature are discussed. No etiology was found for the authors' case.—*J. H. Harris.*

STIEHM, R. H. Early pulmonary tuberculosis and its diagnosis. *Am. J. M. Sc.*, April, 1936, *191*, 542–549.

The routine examination of all freshmen for tuberculosis at the University of Wisconsin is described. It is pointed out that the only way to discovery minimal tuberculosis is by the tuberculin testing of large groups. The positive reactors are fluoroscoped and films made of suspicious cases. Seventy per cent of 1,440 students with positive skin tests had negative roentgenograms; 25 per cent showed first infection type of tuberculosis, and 5.6 per cent showed adult type of tuberculosis. The advisability of periodic examinations by the fluoroscopy of the positive reactors is stressed.—*J. H. Harris.*

BAKER, THOMAS W., and SHELDEN, WALTER D. Coarctation of the aorta with intermittent leakage of a congenital cerebral aneurysm. *Am. J. M. Sc.*, May, 1936, *191*, 626–633.

A case of coarctation in a woman, aged twenty-five, is reported in which the presenting symptoms were neurological and were probably due to intermittent leakage of a cerebral aneurysm. These attacks led to the discovery of the cardinal symptoms of the congenital vascular lesion. The association of congenital cerebral aneurysm with coarctation is emphasized.—*J. H. Harris.*

ABDOMEN

HAFFNER, JOHAN. Fall von verkalktem Aneurysma der Art. Lienalis. (Case of calcified aneurysm of the splenic artery.) *Acta radiol.*, 1936, *17*, 602–608.

A case is described in a woman, aged fifty-one, who for ten years had suffered from obscure digestive disturbances. Roentgen examination showed a rather elongated shadow behind and somewhat lateral from the upper part of the stomach at the level of the second lumbar vertebra. It was about the size of a walnut. It was not connected with the stomach and moved distinctly with respiration. By intravenous pyelography it was found to be independent of the kidney and that it lay laterally from the upper pole of the kidney. Its position

and great mobility indicated that it lay near the spleen and a diagnosis of calcified aneurysm of the splenic artery was made and verified on operation. As there was great danger of a rupture the spleen was removed with the aneurysm. —*Audrey G. Morgan.*

Hansson, Nils. Decalcification of gallstones. *Acta radiol.*, 1936, *17*, 548–550.

During the summer of 1929, a woman, aged twenty-seven, was admitted to the hospital for anemia and splenomegaly. During her stay in the hospital she had a first attack of gallstone colic and roentgen examination showed several small faceted gallstones. On July 1, 1934, she was readmitted on account of pain in the gallbladder region. Roentgen examination showed no gallstones. On opening the abdomen an abscess was found which contained thick pus and two free gallstones. To the median side of this abscess the enlarged, deformed gallbladder was found. It was opened and found to contain stones similar in size and shape to those demonstrated roentgenologically five years before. The operation was successful and the patient recovered. The stones were examined and found to contain so little calcium that they had not appeared in the roentgenogram. Evidently the suppuration in the gallbladder had caused the decalcification of the stones. There may have been a biochemical process similar to that which occurs in inflammation of the bones, where a considerable amount of decalcification always appears in and around the inflammatory process.—*Audrey G. Morgan.*

Allen, William H. Acute pneumonitis. *Ann. Int. Med.*, Oct., 1936, *10*, 441–446.

Pneumonitis is synonymous with bronchopneumonia according to the dictionary but the author believes that clinically and roentgenologically it represents a different group. It is "characterized by signs of respiratory infection, benign course, few physical signs and roentgenographic evidence of a localized pulmonary involvement." During the year 1935, 2,081 cases of respiratory disease were admitted to the Station Hospital, Fort Sam Houston. Of these, 53 were classed as primary lobar pneumonia; 16, as primary bronchopneumonia and 68, as acute pneumonitis. It is likely that more of the latter type would have been discovered had there been more extensive roentgenography; only the most severe cases had chest films. Detailed analysis was made of 50 of the 68 "acute pneumonites." No one causative organism could be associated; it was thought that a filtrable virus was basically responsible, other organisms such as the pneumococcus, type 4 (isolated in a few) being secondary invaders. The average age was 25.5 years, with limits of nine to fifty-one. No deaths occurred; therefore, an exact pathological study was not possible. Ninety-two per cent showed involvement in one or both lower lobes. The characteristic symptoms included cough, fever, malaise and "cold in the head"; occasionally, a dull aching or sensation of fullness in the chest. In no case was there the stabbing type of pain as found in cases of pleural involvement for all of this group showed central lesions. Fourteen per cent complained of sore throat or headaches; 8 per cent, of weakness or chills; 4 per cent, of blood-tinged sputum or of abdominal pains and 1 or 2 cases had a stiff neck, vertigo or night sweats. The temperature ranged from 99° to 105°F. Physical signs were entirely lacking in 20 per cent of the cases; râles were noted in 42 per cent but bronchovesicular breathing in only one. Twenty-four per cent had a leukocyte count of less than 7,000; 30 per cent, between 8,000 and 10,000; otherwise the counts ranged up to 20,000. Roentgenographically these cases showed "a confluent mottled fan or rounded area, usually of homogeneous moderate density in the central portion, with borders fading into the normal lung. It has the appearance of an exudative alveolar infiltration and is usually more localized and of more even density than the bronchopneumonias of childhood or than those which complicate adult diseases." Six per cent of the cases developed complications such as sinusitis, otitis media, peritonsillar infections, etc. The average period of hospitalization was twenty-eight days—including the full period for convalescence. The treatment was mainly symptomatic; fluids and high carbohydrates were forced in most cases and codein used to control the cough.—*A. A. de Lorimier.*

Martin, Lay. Diverticula of the stomach. *Ann. Int. Med.*, Oct., 1936, *10*, 447–465.

Since 1920, five cases of diverticula of the stomach were noted in the Department of Pathology of Johns Hopkins Hospital. In none had the condition been diagnosed before death. The author reports these cases and an

additional one where the diagnosis was made roentgenologically before death. Moreover, he has carefully searched the literature for other cases of true pulsion gastric diverticula. One hundred and three uncomplicated cases are tabulated. They were found at all ages, Broman and Pernkoph each having found one in an embryo and Sinclair, in a four months old child. The majority were found between the ages of thirty to fifty; 54 of the cases were women. The most common location for the pulsion type was near the cardiac opening; 61 per cent were within a few centimeters of it; most of the remaining 39 per cent were distributed along the lesser curvature. Forty-five of these cases were studied histologically; 16 had intact walls; 23, thinned muscularis layers; in 6, the walls showed only mucosa and serosa. In 15 of the cases, pancreatic tissue was found in some portion of the diverticula, usually at the peak. Only one of these was located near the cardiac orifice; 3, along the lesser curvature while the others were in the pylorus. Adenomyomata were found in the walls of 4; carcinoma, in 3 and fibrosarcoma in one. The dimensions of these diverticula varied from a few centimeters in diameter to the size of a fist or even as large as 8 to 10 or even 20 cm. in greatest dimension. Some had constricted pedicles while in others the openings showed the largest dimensions so that the extensions were more pouch like. In 2 cases the openings were found by the use of a gastroscope. Roentgenologically, an ulcer or neoplasm is usually considered. Åkerlund has laid down the following distinctive characteristics: the sac of a true pulsion diverticulum must be mobile; its shadow must be well defined, smooth, regular and must be noted from various angles. Generally, there is no tenderness. In many of the cases it seemed that no symptoms had been associated. Some complained of such disturbances as gas, distention, eructations, pains or gnawing sensations after meals. In some instances these were relieved by taking food or by postural drainages. Among 28 who had had operative excision of the diverticula, relief of symptoms was claimed by 64.3 per cent. Bleeding was noted in only 8 of the cases. In no case did rupture occur. Two or more diverticula were found in 4 of the cases; associated diverticula of the duodenum, in 4 cases; and in 3 of the cases diverticula were also found in the colon. Ulcers were associated in 10 of the cases.—*A. A. de Lorimier.*

ÅKERLUND, ÅKE. Mukozele in der Appendix röntgenologisch diagnostizierbar. (Mucocele in the appendix can be diagnosed roentgenologically.) *Acta radiol.*, 1936, *17*, 594–601.

Meyer and Rockstroh have recently said that roentgen examination is of no value in the diagnosis of mucocele of the appendix. The author describes 2 cases in which it was so diagnosed and gives the roentgen signs as follows: Failure of the appendix to fill with contrast either on the contrast meal or enema. A roundish structure of the density of soft parts in the region of the appendix, the shape of a sausage, kidney or pear with sharp outlines, that may be moved in different directions around the head of the cecum as a fulcrum or may possibly be moved into the surrounding intestinal loops but has no connection with the liver or kidney shadow. Immediately within the outer outline of the soft tissue shadow are superficial calcium deposits giving a picture somewhat similar to that of cholecystitis calcificans.—*Audrey G. Morgan.*

REED, ALFRED C., and ANDERSON, HAMILTON H. Amebiasis and cancer of colon. *Am. J. M. Sc.*, Feb., 1936, *191*, 237–250.

The authors report in detail 4 cases of amebiasis that later developed carcinoma of the colon. They suggest that the malignant process may be initiated by the chronic irritation from the amebic lesion or its products, or it may develop in the polypoid formation and adenomatous growths which follow amebic lesions. It is pointed out that patients who continue to present symptoms after the stools are negative for amebas should be studied carefully for carcinoma of the bowel.—*J. H. Harris.*

MYERSON, A., PURCELL, G. SCHUBE, and RITVO, MAX. Human autonomic pharmacology. V. The effect of acetyl-beta-methylcholine (mecholyl) on the atonic colon. *Radiology*, May, 1937, *28*, 552–558.

In the study of the effect of acetyl-beta-methylcholine (mecholyl) upon the colon it was noted that in 30 mg. intramuscular doses this drug caused a marked increase in the tonicity of the colon and at the same time increased the motility, resulting in increased evacuation rate. It was found that atropine in 1/100 gr. doses banished any effect of mecholyl. The study was made upon patients with dementia praecox and was of an experimental nature only. Clinically the drug is not recommended because of the

unpleasant side effects, i.e., rise in pulse rate, drop in blood pressure, salivation, lacrimation, flushing and sweating.—*J. H. Harris.*

GENITOURINARY SYSTEM

Henline, R. B., and Moore, S. W. Renal arteriography: Preliminary report of experimental study. *Am. J. Surg.*, May, 1936, *32*, 222–229.

Report is made of experiences with various contrast media injected into the aorta of dogs, in an attempt at visualization of the renal circulation. Twenty-one dogs were injected with solutions of sodium iodide of either 50 or 100 per cent skiodan, uroselectan B, thorotrast, iopax or sterile normal saline. The technique of injection is given in detail. The only solution which gave satisfactory arteriograms was the sodium iodide, either 50 or 100 per cent. The arteries were but faintly outlined with thorotrast. Five dogs died shortly after the aortic injections from traumatic hemorrhage. Spasms were noted following the injection of sodium iodide, indicating a sudden shock to the tissues. Three dogs died apparently from the toxicity of the drug. The authors feel that the dangers of the procedure are too great to compensate for the information obtained.—*W. R. Brooksher.*

Kretschmer, Herman L. Sarcoma of the kidney and stone; report of a case and review of the literature. *J. Urol.*, Aug., 1936, *36*, 99–104.

Report is made of the sixth recorded case of sarcoma of the kidney combined with stone. The literature is briefly reviewed and attention is called to the emphasis which various authors have placed upon stone in the production of sarcoma.—*W. R. Brooksher.*

Overgaard, Kristian. A case of internal uroplania. *Acta radiol.*, 1936, *17*, 542–547.

A case is described in a male student, aged twenty-one, from whose right kidney two stones were removed. The incision in the pelvis was barely 1.5 cm. long and was closed with two sutures. About six weeks later he was readmitted on account of hematuria. There was no trace of a concrement but on the operated side there was an irregular shadow extending from a little above the renal hilus down toward the iliac fossa. Its form was roughly triangular; its median margin extended in an almost straight line down in front of the psoas muscle, parallel to and about 2 cm. distant from the spine. On intravenous injection of perabrodil, excretion was normal on the left side. On the right, coincidently with the filling of the pelvis, the intensity of this shadow increased very markedly.

There is little doubt that this was a case of rupture of the kidney pelvis, as a result of which some of the urine escaped through the opening and infiltrated the fatty capsule, constituting an internal uroplania. There was a wound in the fatty capsule through which it escaped and seeped down along the posterior wall of the abdomen, at the same time spreading laterally. —*Audrey G. Morgan.*

Gillies, C. L., and Kerr, H. D. The roentgen diagnosis of lesions of the upper urinary tract; observations on 432 patients having retrograde pyelograms. *Radiology*, May, 1937, *28*, 565–575.

A statistical analysis of 432 retrograde pyelograms is made by the authors. They found infection, tuberculosis, hydronephrosis, renal calculi, ureteral calculi and aberrant hydronephrosis the most common pathological conditions encountered.—*J. H. Harris.*

Wolke, Knut. Pyelogramm mit einem durch einen Nierenarterien-zweig verursachten Füllungsdefekt—pseudodefekt. (Pyelogram with a filling defect—pseudodefect—caused by a branch of the kidney artery.) *Acta radiol.*, 1936, *17*, 566–568.

A filling defect in the kidney pelvis is usually caused by a tumor, a stone poor in contrast or a blood clot. A case is described showing that it need not necessarily be due to any of these causes.

A man, aged sixty-five, who had been operated on in 1911 for a stone in the left ureter came for examination on October 10, 1933, on account of frequent desire to urinate, nycturia and sometimes hematuria. On pyelograms a semilunar filling defect could be seen in the lower half of the right pelvis. It was thought to be due to a local infiltration and the patient was operated on. No change was palpable either in the parenchyma or kidney pelvis, but on closer examination a large, tortuous dilated vessel with rigid walls was found lying over the anterior, lower part of the kidney pelvis. As it was believed that this vessel was the cause of defect seen in the pyelograms the kidney was replaced.

Up to his death in May, 1936, the patient had no further urinary symptoms. His death was caused by bilateral bronchopneumonia. Autopsy showed the kidney and pelvis normal. A large branch of the renal artery lay over the place where the defect had been in the pyelograms three years before.

As there are variations of the renal vessels in 50 per cent of cases it is important to know of this possible cause of filling defect.—*Audrey G. Morgan.*

MIKKELSEN, EJNAR. Huge prostatic calculi in a young adult male. *Acta radiol.*, 1936, *17*, 525–528.

The author reports a case of unusually large prostatic stones in a man aged twenty-two. The roentgenogram had led to the mistaken diagnosis of stone in the bladder. On operation, however, the bladder was found empty while two egg-shaped stones, one as large as a hen's egg and the other smaller, were removed from the prostate. Though a mistaken diagnosis was made in this case, the author thinks that roentgen examination should be made in every case of prostatitis with indefinite dysuric symptoms because of the possibility of prostatic stones.

Prostatic calculi are generally found in old people, most frequently in the form of multiple small stones which are only an incidental finding. There are few reports in the literature of large prostatic calculi.—*Audrey G. Morgan.*

SKELETAL SYSTEM

BAUER, WALTER, and BENNETT, GRANVILLE A. Experimental and pathological studies in the degenerative type of arthritis. *J. Bone & Joint Surg.*, Jan., 1936, *18*, 1–18.

The authors are of the opinion that degenerative arthritis is the result of the wear and tear of increasing age and repeated trauma which may be caused in a variety of ways and that it is not the result of an inflammatory process, metabolic disturbance or endocrine dysfunction. Degenerative arthritis, they believe, is a better term for the disease process called, at various times, hypertrophic arthritis, osteoarthritis, arthritis deformans, or senile arthritis. The word degenerative describes accurately the primary pathological change. The type of cartilage inherited may be responsible for the earlier onset and more extensive changes encountered in one individual as compared with another.

Because of the inability of articular cartilage to regenerate, this type of joint disease cannot be cured. Certain measures, such as weight reduction and correction of faulty mechanics, can be used either to arrest or slow the progress of the degenerative process. The patient can be assured that he will never become a crippled invalid. Joint deformities, subluxations, and restricted motion do occur but such joints never go on to anykylosis. Extensive degenerative joint changes can be present in an individual without necessarily causing important joint symptoms.

Marginal lipping, so frequently demonstrable in roentgenograms, is a late manifestation of the disease, and usually cannot be seen in its early stages. The earliest and primary change in the joints is a gradual and uneven degeneration of the hyaline cartilage of the articular surfaces. This is first seen as a fibrillation of the cartilaginous matrix, which generally begins near the articular surface and is associated with a disappearance of the spindle cell perichondrium. As a result of this fibrillation, which usually takes place at right angles to the articular surface, the neighboring cartilage cells are set free and finally disintegrate and disappear. The original smooth articular surface takes on a papillary appearance. At times, this fibrillation is responsible for the freeing of minute masses of cartilage and fibrilated matrix. Occasionally, only a portion of the articular cartilage undergoes these changes and as a result the cartilage is thinned over a circumscribed area. To meet this erosion and depression, an overgrowth occurs on the opposite joint surface, and an irregular or somewhat toothed joint line is formed and, finally, with ultimate disappearance of the entire articular cartilage, the two bony surfaces are brought into contact. The friction of continued joint motion produces a high degree of polish on the exposed condensed bone which then acquires an appearance closely resembling ivory; hence the term "eburnation of bone."

The authors conclude that if hypertrophic or degenerative arthritis is nothing more than degenerative joint changes due to wear and tear of increasing age, unusual use, or repeated trauma, one has the right to challenge the correctness of the use of the word arthritis with reference to individuals with such joint changes. They therefore propose the name "degenerative joint disease" for this type of joint pathology.—*R. S. Bromer.*

Compere, Edward L. Localized osteitis fibrosa in the new-born and congenital pseudarthrosis. *J. Bone & Joint Surg.*, April, 1936, *18*, 513–523.

Compere reports 2 cases of solitary bone lesions, which were either congenital or occurred in early postnatal life. One was a case of localized osteitis fibrosa of the proximal third of the tibia and the other was a typical congenital pseudarthrosis in the lower third of the tibia. Both cases resulted in fracture and non-union. Four similar cases have been reported in the literature. Three of these were described as cystic lesions. In the fourth case, there was no operative interference to demonstrate the presence or absence of cyst formation, and no fracture occurred.

In his first case, bowing of the tibia was noted, suggesting that this lesion may have stimulated longitudinal growth from the proximal tibial epiphysis so that the tibia became relatively longer than the fibula and bowed, due to lack of support on the lateral side where the defect in the bone was most extensive. Union was obtained, followed by normal function, through the use of full-thickness tibial bone grafts. Each of his cases, Compere thinks, adds support to the contention of Stierlin, von Beust and Fragenheim that fibrous or cystic disease of the bone is the underlying cause of congenital pseudarthrosis.—*R. S. Bromer.*

Wortis, Herman. Osteopetrosis ("Marble bones"). *Am. J. Dis. Child.*, Nov., 1936, *52*, 1148–1157.

The characteristic evidence of osteopetrosis is the roentgen demonstration of the overgrowth of the cortical portion of the bone at the expense of the medullary cavity. This condition is usually most noticeable in the central portions of the pelvic bones, the bodies of the vertebrae, the bones at the base of the skull, the upper end of the femur and the lower end of the tibia and fibula. Certain secondary manifestations usually, although not invariably, accompany the disease process. They include multiple fractures, chronic osteomyelitis, epiphyseal deformities, physical underdevelopment, hydrocephalus, atrophy of the optic nerve, imperfect dentition, anemia and various leukemic states, and metaplasia of the bone marrow elements leading to enlargement of the liver, spleen and lymph nodes.

The causative factor of osteopetrosis is unknown. It does, however, show a striking familial tendency and is occasionally hereditary. Parental consanguinity is apparently a factor. The endocrine glands were involved in only one case reported in the literature where a parathyroid tumor associated with renal concretions complicated the bony involvement. The disease process is a disturbance of the endosteal and endochondral bone metabolism, the periosteum remaining almost always intact. There may be associated evidence of active or old rickets. There is an increase of the hard cortical bone to more than twice its normal thickness, with condensation and broadening of the bony trabeculae, obliteration of the spongiosa by the encroaching compacta and crowding of the elements of the marrow, often with replacement of the latter by fibrous tissue.

On roentgen examination, the bones are usually dense, with obliteration of the marrow cavity. These changes are almost universal but are most marked in the vertebral bodies, the base of the skull, the upper ends of the femurs and in the lower ends of both tibias and fibulas. The sella turcica is usually narrowed and the posterior clinoid processes show a clublike thickening. Irregularity of the epiphyseal line is frequently noted. Centers of ossification usually appear at the normal time or are slightly delayed, and the union of the epiphysis with the shaft is only occasionally subject to delay. Ossification of the cranial sutures is often delayed. Striations consisting of alternating transverse bands of exceedingly dense and more nearly normal bone occur most often in the distal parts of the long bones. These changes are usually manifest in infancy.

Chemical analysis of the diseased bones has revealed no marked deviation from the normal. The prognosis is dependent on the age at which the disease makes itself manifest clinically, being much more severe in infants, and also on the gravity of the secondary manifestations.

Wortis reports a case of a boy, aged nine, who presented roentgen changes indicative of marble bones but who showed none of the secondary changes. There was no hereditary history. The prognosis in his case was thought to be fairly good because of the patient's age and the lack of complicating factors. The roentgenogram, among other changes, showed marked thickening of the bones of the base of the skull and narrowing of the sella turcica with clublike clinoid processes.

His patient presented a behavior problem but Wortis feels that the osteopetrosis has played no part in these personality changes. That he had an apparently faulty "anlage" is evidenced by: (*a*) vascular anomalies of the face, the left side of the palate and the left ear drum; (*b*) inguinal hernia on the right side and clubfoot at birth; (*c*) undescended testes, and (*d*)"marble bones."—*R. S. Bromer.*

COMPERE, EDWARD L. Pathologic and biochemical changes in skeletal dystrophies; analysis of results of treatment of parathyroid osteosis. *Arch. Surg.*, 1936, *32*, 232–272.

This review of the relationship between parathyroid disease and the more common skeletal dystrophies contains considerable valuable information. The study is based upon the clinical and biochemical findings in 124 patients with proved hyperparathyroidism, and may therefore be considered authoritative.

True parathyroidism is associated with adenomatous tumors of one or more parathyroid glands. The disease is progressive, producing weakness, generalized bone demineralization, fractures, pain, and disabling deformities. Multiple foci of osteitis fibrosa, with or without giant cell tumors and cysts, also characterizes the condition.

This osteodystrophia referred to by Compere as parathyroid osteosis is almost invariably associated with elevated serum calcium figures and low plasma phosphates. These chemical determinations, when coupled with negative calcium balance studies, are of paramount importance in the diagnosis of true hyperparathyroidism. The importance of these findings may be appreciated when one considers the many diseases with bone changes from which it must be differentiated. The similarity between the roentgen findings in parathyroid disease and osteitis fibrosa, Paget's disease, osteogenesis imperfecta, osteomalacia and ankylosing polyarthritis, frequently causes confusion.

There is no good evidence that Paget's disease is related to hyperparathyroidism. In this condition, the normal calcium and phosphate contents of the blood and the markedly positive calcium balance point against this relationship. Ankylosing polyarthritis is probably not caused by hyperparathyroidism, although the calcium content of the serum may be slightly elevated. In these cases, normal inorganic phosphates and a positive calcium balance may be taken as good evidence against primary parathyroid disease even though the parathyroid may sometimes be enlarged. The demineralization described in polyarticular arthritis may be accounted for on the basis of atrophy of disuse. Certainly, there is no conclusive evidence to justify parathyroidectomy in such cases.

The author stresses the importance of early diagnosis in patients with true parathyroid osteosis to prevent visceral and skeletal changes which, in advanced cases, are irreparable.

The article has an excellent bibliography which deals with parathyroidism and the other osteodystrophies.—*P. J. Hodes.*

DALL'ACQUA, V., LEVI, P., and BORDOLI, L. Osteopatia generalizzata a molteplici strie simmetriche di riassobbimentosindrome de Milkman. (Generalized osteopathy with multiple symmetrical absorption stripes—Milkman's syndrome.) *Radiol. med.*, Oct., 1936, *23*, 733–749.

A case is described in a woman, aged forty-three, who had suffered for about four years from discontinuous pain which appeared at first in the legs and then extended to the upper part of the skeleton, particularly the clavicles, the sternum and the arms, and also to the sacrum. On roentgen examination the authors found multiple bone changes.

These lesions appeared in both the long and flat bones. They were in the form of transparent stripes 3 to 4 mm. broad, caused by absorption of bone. They resembled the picture of fractures but there was never any displacement of the apparent fragments. They ran transversely across the bones. In some cases, the whole thickness of the bone was affected, both compact and spongy tissue being involved, in some only a part of it. These stripes were seen in the epiphyses and metaphyses as well as in the diaphyses. In some places there were multiple localizations in the same bone. There was generally a slender border of thickened bone surrounding the pseudo-fractures. In most of the foci there were no signs of periosteal reaction, and when they did occur they were slight. In a general way, the lesions were symmetrical, that is, corresponding areas were affected on the two sides, but not in exactly the same sites or to the same degree.

Clinical and roentgen examination did not show any special lesions of the viscera. Laboratory examinations showed increased phosphates in the blood.

The authors discuss the differential diagnosis of this disease from rickets, osteomalacia, congenital and late osteogenesis imperfecta and multiple myelomata of the bones, and conclude that it is a pathological entity distinct from any of these diseases. Only 2 cases have previously been described in the literature—those of Milkman in 1930 and Michaelis in 1932.

The disease seems to begin in the second or third decade of life or even later. Milkman believes that though its course is very slow, it is progressive and fatal. Nothing is known in regard to its etiology.—*Audrey G. Morgan.*

Schwarz, Gabriel A., and Wigton, Robert S. Fracture-dislocations in the region of the atlas and axis, with consideration of delayed neurological manifestations and some roentgenographic features. *Radiology*, May, 1937, *28*, 601–607.

Two cases are reported which presented neurological symptoms some years after trauma to head and neck. In one case the history of the injury was not obtained until the fracture-dislocation of the 1st and 2nd cervical vertebrae was discovered by roentgen examination. The cause of the clinical symptoms is not known. A laminectomy was performed on one of the cases. No evidence of pressure was found and there was only moderate improvement following the operation. The authors recommend careful roentgen study of the atlanto-axial region in all uncertain cases of spastic paraplegia, even without a history of trauma to the neck or without local signs and although the nervous symptoms and signs are far removed in time from a known injury.—*J. H. Harris.*

Oppenheimer, Albert. Diseases affecting the intervertebral foramina. *Radiology*, May, 1937, *28*, 582–592.

The normal anatomy of the intervertebral foramina and the technique of roentgen examination are discussed. The value of oblique views of the cervical and lumbar spine is emphasized. The narrowing of the foramen is due either to a breakdown of the tissue that normally holds in place the bones encircling the foramen or by the formation of tissue which encroaches upon the lumen (constriction). The collapse may result from thinning of the intervertebral discs (discogenetic disease) due to rupture of the annulus fibrosus and fracture or contusions of the vertebrae. The narrowing of the intervertebral space thus produced causes a collapse of the anterior half of the intervertebral foramen followed by anterior subluxation of the superior articular process of the subjacent vertebrae. Rarefaction of the articular process, etiology unknown, results in a narrowing of the posterior half of the foramen.

Constriction of the foramen may be due to primary arthritis of the apophyseal joints (spondylarthritis). In the early stages there is soft swelling of the periarticular structures but later calcification occurs with the resulting spur formation.

These types of narrowing can be determined by the roentgen examination. This is an excellent article and contains a number of cuts exemplifying the condition described.—*J. H. Harris.*

Shlionsky, Herman, and Blake, Francis G. Arthritis psoriatica; report of a case. *Ann. Int. Med.*, Oct., 1936, *10*, 537–546.

This report is of a housewife, aged fifty-seven, who had been troubled with psoriasis and joint lesions over a period of twenty years. The background was negative for tuberculosis, syphilis or gonorrhea. When her joint lesions first developed there was made a questionable diagnosis of rheumatic fever. She was bedridden for about a year, during which time all of her teeth gradually fell out. The rash which appeared psoriatic, was generalized and was refractive to treatment, though it cleared during the months of July and August. The joint lesions continued and the deformities progressed in severity. The blood Kahn was negative. The spinal fluid was negative. The total serum proteins were 7.61 per cent; albumin, 4.11 per cent; globulin, 3.50 per cent; calcium 8.74 per cent; phosphorus, 4.01 per cent. Hemolytic streptococcus agglutination tests were negative. Roentgenographically, the most striking changes were found in the distal ends of the extremities, though milder changes were also noted in the more proximal portions. All bones showed deossification. Many showed a concentric atrophy with thinning of the cortical compact bone and coarsening of the trabeculations. The shoulders showed osteochondritic changes, with irregular areas of rarefaction and condensation in the head of the humerus. The clavicles showed a tapering of the outer ends. The knees showed proliferative changes especially along the superior aspects of the patellae. The elbow joints were narrowed; the olecranon processes appeared spongy. Tapering

was also seen in the extremities of the ulnae and of the head of the radius. The proximal carpal bones, with the exception of the pisiform, were missing from the left hand, and the distal carpal bones were fused into a contracted flattened mass. The carpometacarpal joint spaces were obliterated and the metacarpals showed tapering and loss of the heads. The proximal portions of the proximal phalanges were also tapered; the distal phalanges showed marked deossification. Because of the tapering all parts of the extremity were shortened with buckling of the soft tissues. The right upper extremity showed similar changes, as did also the tarsals, metatarsals and phalanges of the feet.

Other cases such as this one have been reported. Some observers believe the arthritic phase to be peculiar to psoriasis; others consider it a primary infectious arthritis. It is likely that the joint and the skin conditions are at least etiologically related.—*A. A. de Lorimier.*

GUTMAN, ALEXANDER B., and KASABACH, HAIG. Paget's disease (osteitis deformans). *Am. J. M. Sc.*, March, 1936, *191*, 361–380.

The authors review their experience with 116 cases of Paget's disease. The conclusion is drawn that the diagnosis rests upon the roentgen findings. The serum phosphatase was quite high in all cases examined with one exception. This chemical finding occurs in other bone conditions, particularly osteoplastic prostate metastasis, hence is no aid in making a differential diagnosis.—*J. H. Harris.*

ROENTGEN AND RADIUM THERAPY

LAMMERS, H. Hyperintensive Bestrahlung bestimmter Krebsformen. Betrachtungen und vorläufige Erfahrungen. (Hyperintensive irradiation of certain forms of cancer. Discussion and preliminary experience.) *Strahlentherapie*, 1935, *52*, 51–60.

The author's method of treatment is based on a single very intense irradiation. There are two methods of increasing the intensity of the rays—by increasing the strength of the current and decreasing the focus-skin distance. He chose the latter method. As a rule, electrical high tension is an obstacle to shortening the focus-skin distance beyond a certain point. This danger was overcome by the use of the new Philips installation with complete protection from radiation and high tension. He has irradiated patients without any danger with 200 kv. and 4 ma., and with a focus-skin distance of 16 cm. or less, in some cases as low as 11 cm. In this way, the intensity at the surface of the body was increased to three times or more the maximum that is usually given. Of course this intensity affects only the superficial tissues; there is a very rapid decrease toward the deeper tissues and so this method is not adapted for the treatment of deep-seated cancers, such as those of the uterus, rectum and prostate. These are the forms for which Coutard's protracted fractional irradiation is indicated.

The form of cancer for which this intensive method was best adapted seemed to be the cancerous proliferation in the superficial lymph tracts of the anterior and lateral walls of the thorax following cancer of the breast. They consist of rapidly proliferating cells with a high karyokinetic index. They are therefore very radiosensitive.

Six cases are described in which this method was used. They were of course hopeless cases and the method was only palliative. They are reported only for the sake of improving the method and finding the types of cases in which it can be used with better prognosis. The skin metastases were cured in these cases.

The advantages of the method are its short duration, so that the danger of proliferation and dissemination of the cancer cells is overcome; the fact that it does affect only the superficial tissues and there is no danger of injuring deep-seated vital organs and that these rays of high intensity seem to have a cancericide action that is different qualitatively from that of other forms of irradiation.—*Audrey G. Morgan.*

BORAK, J. Über regionäre Hautreaktionsunterschiede. (Regional differences in skin reactions.) *Strahlentherapie*, 1935, *52*, 74–84.

Cases are described which illustrate the varying degrees of sensitiveness to irradiation of the skin at different sites. This different sensitiveness is seen not only in the skin but also in the blood vessels. Skin which lies over bone or vessels which lie adjacent to bone show much weaker reactions than ones that are surrounded by soft parts. This is true both of transitory early reactions and of late reactions.

These differences in reaction cannot be explained on the basis of irradiation physics, such as differences in absorption and back-scattering of the rays. They must therefore be due to

differences in sensitiveness of the tissues in question to the rays. Probably vessels lying near bones are subjected to greater pressure than those surrounded by soft parts. Experiment has shown that when vessels are subjected to compression they and the tissues supplied by them show decreased sensitiveness to rays. —*Audrey G. Morgan.*

Sarasin, R. Haut- und Schleimhautreaktionen bei protrahiert-fraktionierter Röntgenbestrahlung. (Skin and mucous membrane reactions in protracted fractional roentgen irradiation.) *Strahlentherapie*, 1935, *52*, 61–73.

Cases of protracted fractional irradiation of tumors of the upper respiratory tract are described which show that the reaction to the same dose varies greatly in different individuals. The technique should be carefully adapted to the individual case and the rhythm of irradiation that proves best adapted to the case should be carefully observed and strictly adhered to. The skin and mucous membrane reactions do not run parallel. A case is described in which with rather low dosage there was an intense mucous membrane reaction and only a slight skin reaction. The results were good.

The mucous membrane reaction generally begins on the sixteenth to twenty-first day after the beginning of treatment and reaches its maximum in about four days. If it appears earlier or is too intense the dosage should be decreased. A mucous membrane reaction is necessary for the success of protracted fractional irradiation. There is a definite relationship between the radiosensitiveness of the tumor and that of the mucous membrane, but the radiosensitiveness of the skin is independent of both.

The reactions of both mucous membrane and skin can be decreased by different methods, such as the use of short wave treatment and infra-red irradiation. Decrease of the mucous membrane reaction in this way does not decrease the effectiveness of the treatment. On the contrary the author has found short wave therapy a valuable supplement in helping the normal tissue in its resistance to the disease.—*Audrey G. Morgan.*

Pochy-Rianò, Roberto. Elettrolisi o diatermocoagulazione nella cura dei tumori vascolari del viso. (Electrolysis or diathermocoagulation in the treatment of vascular tumors of the eye.) *Arch. di radiol.*, Mar.-Apr., 1936, *12*, 121–133.

The author discusses the nature of electrolysis and diathermocoagulation and their comparative value in the treatment of tumors. Surgical diathermy is based on the passage of a high frequency electrical current through special operative electrodes. It destroys the pathological tissue by means of heat.

A case is described in which this method was used for the removal of a cavernous hemangioma of the upper eyelid in a child a year and a half of age. Two months and a half after the treatment the child showed no trace of the tumor. There was no general or local reaction, the cosmetic result was excellent, and the child is still free of symptoms after three years.

The author believes that this method of surgical diathermy should be more widely used than it is.—*Audrey G. Morgan.*

Hermann, Hanns-Hein. Zu den Röntgenschädignungen der Parotis. (Roentgen damage of the parotid gland.) *Strahlentherapie*, 1937, *58*, 220–229.

In a patient receiving roentgen irradiation for carcinomatous involvement of the hypopharynx, the necropsy findings disclosed marked pathologic changes in the parotid gland, on the side directly in the field of the maximal radiation. This phenomenon, namely lipomatous degeneration of the parotid gland, had not been noted in the author's experience heretofore, and experimental studies were instituted to determine whether intensive radiation therapy over the parotid gland could cause impairment or permanent damage to its function and structure. Further, it would be of value to determine if there was any definable difference in reaction of the salivary glands to various types of roentgen treatment; and to establish the method which was least inimical to their function. Conducting experiments upon rabbits with relatively analogous doses to those used in humans the author concluded that the radiosensitivity of the normal parotid gland was slight as contrasted to other glands. He was strongly of the opinion that the lipomatous changes noted in the above autopsy findings were not and could not be produced by radiotherapy, even if conducted beyond the point of skin and tissue tolerance. The commonly noted clinical symptoms of dryness of the mouth and throat, edematous painful swelling about the

irradiated salivary glands, are in most instances merely transient complaints and he personally had never experienced a permanent alteration of normal physiological function. This factor is readily perceived to be of inestimable value in the treatment of parotid fistula in that eventually no residual damage to the glands will ensue.

No appreciable difference in reaction to the various types of irradiation was discernible, and therefore from a purely economic standpoint it would seem more feasible to utilize the simple fractional method, as compared to the protracted fractional method.—*W. R. Stecher.*

ALBRIGHT, HORACE L. Cancer of the face, especially of the region of eye. *Am. J. Surg.*, Aug., 1936, *33*, 176–179.

The author presents a method of treating malignant skin lesions up to 3 cm. in diameter based largely upon the experience of the Radiumhemmet, an epidermicidal dosage of 7–10 S.E.D. being given, a stable scar with minimal deformity and better cosmetic result being the usual course. Radium element needles, filtered with 0.5 mm. platinum are employed, either six of 10 mg. strength, or eight of 3 mg. strength, the treatment usually requiring four hours. Persistent induration after six weeks must be strongly suspected as tumor, requiring additional treatment of less intensity. Lesions larger than 3 cm. are considered best controlled by surface irradiation by lightly filtered roentgen rays, or by the radium bomb of 5 gm. at 3 cm. distance, or by wide excision with pedicle flap repair. Care must be taken in the irradiation of lesions close to the eye to avoid cataract formation, tear duct stenosis, ectropion and corneal ulceration.—*W. R. Brooksher.*

FRANK, I. WALLACE, ENFIELD, C. D., and MILLER, A. J. Rhabdomyosarcoma of the neck. *Ann. Surg.*, Sept., 1936, *104*, 431–435.

Report is made of a case of rhabdomyosarcoma occurring in the neck, operated upon the second time for local recurrence. Roentgen irradiation was employed, giving 1,320 r to each of three fields in the first series, and 945 r to each field in the second series. Roentgen study prior to operation disclosed bone destruction in the cervical vertebrae. When last heard from, the patient was perfectly well.—*W. R. Brooksher.*

KAPLAN, IRA I. Radiation therapy of malignant lesions of the lip. *Radiology*, May, 1937, *28*, 533–543.

The technique of treatment of cancer of the lip at Bellevue Hospital is described. In the event there is gland involvement this is treated before the local lesion is attacked. The glandular area is treated by external irradiation with roentgen rays or radium pack and the residual gland is either removed or interstitial irradiation is given. In the event that dissection of the nodes of the neck is planned preliminary irradiation is given (900 r with 200 kv. (peak) and 0.5 mm. Cu filtration) and the surgery is done three weeks later.

The local lesion is treated by external or interstitital irradiation with radium. For the local application of radium, molds of wax or rubber are prepared in which is incorporated lead to protect the surrounding healthy skin. Filtration is 1 mm. of platinum and the dosage ranges from 1,000 to 2,500 mg.-hr. For interstitial irradiation either removable needles or gold seeds are used. If needles are selected, the dosage is 1,000 to 3,000 mg-hr. and if seeds are used, the dose is 50 to 133 mc-hr. per cubic centimeter of involved tissue.

For the large ulcerated lesions intensive superficial roentgen irradiation is used.

The results in 100 cases compare favorably with those following surgery with the added advantage of no immediate operative mortality. The mutilating scars are much less likely to occur following irradiation.—*J. H. Harris.*

MARTIN, HAYES E. Peroral x-radiation in the treatment of intra-oral cancer. *Radiology*, May, 1937, *28*, 527–532.

The description of a method of treating intraoral cancers at the Memorial Hospital is given. The general plan is to give daily doses of roentgen radiation to be supplemented by interstitial radon implants. When possible, lead-lined cones 4 cm. or less in diameter are used intraorally and thus a minimum of normal tissue is irradiated; 200 kv. (peak) is used at a distance ranging from 65 to 35 cm., depending upon the estimated depth of the lesion. The roentgen beam is accurately directed in order to include the entire tumor in the field.

The dosage varies with each case but as an example, a lesion 2.5 cm. in diameter in an average situation would be given 200 to 250 r daily for twenty days after which 6 to 8 mc. in seeds would be implanted immediately.

The use of small localized areas perorally has materially reduced the incidence of osteomyelitis and late radionecrosis.—*J. H. Harris.*

Hess, P. Die Röntgenbehandlung der Hyperthyreosen. (Roentgen therapy of the hyperthyroses.) *Strahlentherapie*, 1937, *58*, 74–82.

The author presents a ten-year survey, and concludes that the results of roentgen therapy in the hyperthyroses are very difficult to evaluate in an absolute sense, for one cannot always determine whether the symptoms manifest are primary or secondary to other factors, such as neuropsychopathia or related endocrine dysfunction. Unquestionably, as statistics confirm, if the hyperthyroidism is primary, then the results are excellent; and, conversely if secondary, the results are patently not as favorable. The work convinced the author, that as intimated, in various pharmacologic experiments, there is a definite hypophyseal thyrotropic hormone, which factor adds great confusion to the original diagnosis. The hyperthyroses are divided pathologically into: (1) primary Basedow's disease; (2) mesencephalic Basedow's disease, which is very resistant to any form of therapy and clinically strongly resembles true morbus Basedow; (3) hypophyseal Basedow's disease, frequently occurring during the menarche.

The following clinical classification was employed and the author's results are as tabulated:

	Cured	Improved	Uninfluenced
Thyrotoxicosis	40.5%	34.5%	25.0%
Struma Basedowificata	48.0%	39.0%	13.0%
Basedow(classic)	50.0%	37.0%	13.0%
Total	47.0%	37.0%	16.0%

Thus, in the thyrotoxicosis category, the rather poor results are accounted for by assuming concomitant hypophyseal, mesencephalic, or pluriglandular forms, whereas, in Basedow's disease a pure thyrogenic origin is approached. In all types, thyroid enlargement was definitely reduced, and the greatest effect noted in the thyrotoxicosis type was the lessened general symptoms; in struma basdowificata, the local symptoms; and in classical Basedow's disease, the accompanying cardiac symptoms.

General considerations in roentgen therapy stipulated the following: The more advanced and severe the case, the smaller the single dose, and the increased fractionation, and greater the cumulative dose. Three to four thousand roentgens are administered; usually 150–180 r per sitting; and six sittings over a three-week period constituting a series. A total of two to three series is given with intervals of six to eight weeks. Curiously, the most severe cases responded to roentgen therapy with the best terminal results.

The author stresses the need for great psychological tact in order to keep the patient under control and thereby to continue with the protracted roentgen therapy, which becomes very trying to the patient, who generally is very impatient and desires immediate results. No mortality occurs with radiation therapy, and in certain cases this method of therapy was the only method which afforded results.—*W. R. Stecher.*

Brünauer, S. R. Zur Anwendung der Radiumschwachtherapie in der Dermatologie. (The use of weak radium therapy in dermatology.) *Strahlentherapie*, 1937, *58*, 83–93.

Radium emanation salve is employed, which is made by intimately mixing a salve base with radium emanation in specified amount; thus, one tube of ointment contains in the application stage, the activity of 100 electrostatic units which is equivalent to 100,000 millistat. The radon salve is applied on the affected part, knife blade in thickness, covered with guttapercha and retained by adhesive plaster. It is applied two to three days, and during the interim of one to two days, an indifferent salve is applied. It is frequently necessary to administer the salve over a period of ten to fifteen days, and a slight erythema may be produced. The one distinct advantage of radon salve is its ease of application to parts such as between the toes and fingers. In eczema interdigitale pedum, and pruritus ani, no covering is utilized. Approximately 92 per cent of the energy is emitted in the form of alpha rays; 6 per cent in beta; and 2 per cent in gamma rays, which accordingly accounts for its salubrious superficial action.

Metallic compresses containing radium in the form of varnish (9×12 cm. plaque containing 1 mg. radium bromide) is advantageously employed in its ability to be molded to the affected part, and offers a better uniform radiation distribution. The technique consists of 3–6 applications, each of twelve hours' duration, and an interval of fourteen days in which the indifferent salve is employed. The treatment

series is terminated with a similar cycle or a full or one-half strength dosage. The name for this type of therapy should be "weak radium-ray therapy" rather than "weak radium therapy."

In eczematous dermatitis comprising chronic eczema, lichen chronicus Vidal, eczema interdigitale pedum, eczema ad genitale, eczema and pruritus ani, eczema meatus auditorii externi, neurodermitis chronica, in a series of 36 cases, 20 were completely cured, and 8 greatly improved. Four of the unimproved were benefited by further therapy, constituting a third course.

In psoriasis vulgaris, 5 cases in a group of 9 were completely cured, 2 were improved and 2 unaffected. Three cases of lichen ruber planus were cured. In a final group including various conditions such as herpes zoster, angioma, fibroma, papilloma, verruca vulgaris, and planae juvenilis, the results were difficult to evaluate on account of the time interval necessary for true evaluation, and also the response without therapy in cases of herpes zoster; but in general most cases were at least benefited. In a case of multiple papillomata affecting the bearded region of the face, excellent results were obtained by radon salve.

In concluding, the author stresses the fact that this type of therapy is the method of choice, particularly in circumscribed eczematous interdigital lesions, psoriatic dermatologic affections, hyperkeratoses and rhagades, and lichen ruber planus. In these the radon salve is preferable. This method is applicable where ordinary roentgen irradiation and grenz-ray therapy are impractical on account of location. In addition the factor of fear of some patients of roentgen rays and radium is overcome by the use of radon salve in its stead. The radon salve is cheap, and the radium plaques are clean, and afford exact dosage.—*W. R. Stecker.*

Del Buono, P. Über die rationelle Röntgentherapie der akuten, nichteitrigen Entzündungen des Rückenmarks. (Roentgen therapy in acute, non-suppurative inflammatory conditions of the spinal cord.) *Strahlentherapie*, 1937, *58*, 251–266.

The author evaluates his personal experience and that of other observers who have employed roentgen therapy in acute anterior poliomyelitis in children, acute and chronic poliomyelitis in adults, and acute and chronic multiple sclerosis. Unquestionably there is some beneficial action of radiation in all non-suppurative acute inflammatory lesions involving the spinal cord; and in most instances better results are obtained by this method than any other therapeutic procedure. He found the best results to be attained in acute anterior poliomyelitis in children, but only when therapy was instituted early, i.e. before permanent and extensive lesions of the cord became manifest. Some good results were obtained in adults with anterior poliomyelitis, as was also noted in acute multiple sclerosis, and radiculomyelitis. However, since most of these entities were treated late, the results were not comparable. Chronic multiple sclerosis is definitely radioresistant.

It is to be remembered that improvement in these cases may not be apparent for some time after commencing treatment, and even then may not be permanent. In all instances, where a recurrence of symptoms occurred, continued radiotherapeusis was ineffective, and did not check the advance of the infection. Curiously, of the numerous techniques employed, the general terminal results were approximately similar; the most important factors being the radiosensitivity of the involved spinal cord parenchyma, and the absorption coefficient of the skeleton as exemplified in the various age groups. Deductively, it was established that the most rational technique was an empirical minimal dosage conducive to efficacy. The author was not acquainted with one case in the literature in which permanent damage to the spinal cord could be attributed to the effects of the irradiation, and in many cases very high total dosage was administered.—*W. R. Stecher.*

Edling, Lars. Über Frühresultate von Teleradiumbestrahlung bei Karzinom des Larynx und Hypopharynx in Lund 1931–1933. (Early results of teleradium treatment of carcinoma of the larynx and hypopharynx in Lund from 1931 to 1933.) *Strahlentherapie*, 1935, *52*, 206–215.

Since 1930 the author has had the use of 2 gm. radium for teleradium treatment of tumors of the larynx and hypopharynx. The details of the application of the radium are described. The regular daily dose that is given when the patient's condition permits it is 4,880 mg-hr. With this dosage the total time required for treatment is sixteen to twenty-four days. The total amount in this series of cases has varied from 52,000 to 90,000 mg-hr.

Generally the patients bear the treatment very well. But toward the end in the majority of cases there are some general symptoms, such

as fatigue and in some cases nausea, rarely vomiting. These symptoms seem to be milder than after protracted roentgen treatment and to stop sooner after treatment is discontinued. The local effects are similar to those in protracted fractional roentgen treatment.

Eight cases of carcinoma of the larynx were irradiated and 5 of the patients are still living and free of symptoms after three and a half, two, one and a half, one and a third and one year. In Case 1 a small local recurrence developed a year and a half after treatment which was promptly removed by laryngofissure and electro-endothermy. Since then the patient has been completely well. There were no complications in the other cases. The function of the larynx in all these cases is very good.

Among the 10 patients with carcinoma of the hypopharynx treated, 3 are still living and free of symptoms four, three and a half and two years after treatment. Most of these cases come for treatment late when they are inoperable.

Most of the deaths in these cases (3 of cancer of the larynx and 5 of cancer of the hypopharynx) were caused by local recurrence or residual tumors. Two of the patients with cancer of the hypopharynx died during or soon after the treatment of dyspnea or aspiration pneumonia. In one case the recurrence was operated on by electro-endothermy but with poor results—death after two months. In one case of cancer of the hypopharynx late distant metastases were the cause of death.

The author considers his experience with teleradium very encouraging. The cases were not selected except that those cases were rejected in which there were such extensive metastases in the cervical glands that teleradium treatment was difficult technically. The results in carcinoma of the larynx compare well with those of surgery as far as cure of the tumor is concerned. And the functional results are much better, particularly in the cases in which laryngofissure would have had to be performed. And in addition to that, teleradium is an effective treatment for any present or future metastases. In this it is also superior to other methods of radium treatment, especially the fenestration technique of Seifert. But it must be admitted that the local and general symptoms are a severe tax on the patient for several weeks. In cancer of the hypopharynx in which surgery, even in the most skillful hands, only exceptionally brings about complete cure and generally results in severe mutilation which makes the patient's life a martyrdom, radiotherapy is without doubt the treatment of choice.

The author believes that teleradium, where it is indicated technically, is superior to protracted fractional roentgen treatment because it has a better biological effect on the tumor and there is less danger of injury by the irradiation. Neither in this material nor in teleradium treatment in general has the author noticed the heart symptoms that have been described after large doses of roentgen radiation.

It remains for the future to show whether these cures will be permanent. The results of any treatment in tumors of the hypopharynx are still far from satisfactory. Possibly they will be improved by further advances in teleradium technique. More homogeneous irradiation could be obtained with longer focus-skin distance. Attempts should also be made to change the temporary freedom from symptoms into permanent cure by carefully increasing the dosage. —*Audrey G. Morgan.*

Coutard, H. Über Röntgentherapie der Pharynxkarzinome. (Roentgen treatment of carcinoma of the pharynx.) *Strahlentherapie*, 1935, *52*, 1–10.

The author reports the roentgen treatment of 89 cases of carcinoma of the hypopharynx treated from 1921 to 1926. On Jan. 1, 1934, the shortest observation time for any of the living cases was eight years. After one year there were 55 survivors (61 per cent), after two years 30 (33 per cent), after three years 14 (15 per cent), after four years 14 (15 per cent), after five years 11 (12 per cent), after six years 10 (11 per cent), after seven years 8 (9 per cent). For the first three years the curve of deaths was almost perpendicular, after that almost horizontal. The number of survivors fell from 30 at the end of the second year to 14 at the end of the third year. Of the 16 deaths 11 were from local recurrence, 2 from lung metastasis and 3 from abdominal metastasis. Between the fourth and fifth year one died of lung metastasis and one of liver metastasis, during the sixth year one of lung metastasis and during the seventh year one of lung metastasis and one of abdominal metastasis.

In most of the cases the dosage was 6,000 to 8,000 r measured at the skin. The average size of the fields was 75 to 125 sq. cm. The tension was up to 200 kv., the filter 2 mm. zinc and 3 mm. aluminum. The focus-skin distance va-

ried from 40 to 60 cm. The dose in all cases was "epithelicide," that is, it caused radioepithelitis of the mucous membranes and radioepidermitis of the skin.

The cases that were cured were not infiltrating ones. They were all movable on the underlying tissues. No cures were brought about in cases in which the muscles were completely infiltrated.

The essential factor in cure seemed to be not increase in dosage but lengthening of the time during which the dose was applied. The important thing seems to be protection of the tumor bed rather than local destruction of the cancer cells. They have frequently found that a tumor receded less rapidly in the parts that were given large dosage and the stroma injured than in parts where the irradiation was not so strong and the stroma was relatively little injured.—*Audrey G. Morgan.*

MÜLLER, ROLAND. Über die Radiumbehandlung des Stimmbandkarzinoms vermittles der Fensterung. (The radium treatment of carcinoma of the vocal cords by fenestration.) *Strahlentherapie*, 1935, *52*, 216–220.

Halberstaedter and Seiffert in 1930 reported their method of radium treatment of carcinoma of the vocal cords by fenestration of the laryngeal cartilage with insertion of a plate carrying the radium.

The author describes his use of this method. For the past two years two kinds of plates have been used. One has an irradiating surface of 1.7×1.3 cm. and holds 6.5 mg. radium uniformly distributed. It is filtered with 1 mm. gold. The surface turned away from the tumor is covered with 1 mm. lead. This is the one ordinarily used. A second carrier of the same size, used chiefly for tumors that leave the anterior third of the vocal cord free, is divided into three cells that contain from in front backward 1, 2 and 3 mg. radium. This spares the normal anterior commissure. The plates are left in place for eight to nine days. The total dose is about 1,300 mg-hr. The tissues will bear more than that.

Eleven cases of tumor of the vocal cords have been treated in this way in 1933 and 1934. In 10 of them the tumor disappeared. In one case the tumor had to be extirpated before the reaction was completed. There were no complications during the treatment. There was occasionally considerable swelling of the mucous membrane, especially of the aryepiglottidean fold. But this never necessitated a preliminary tracheotomy or a supplementary operation afterward. There were no disturbances of healing of the wound after the plate was removed. In all the patients function of the vocal cords was preserved. In some cases there was a certain sensitiveness to external stimuli that caused transitory hoarseness. There was no skin reaction.

Of the 5 patients treated in 1933, four, or 80 per cent are alive and free of symptoms after one to two years. All of the 6 treated in 1934 are alive and free of symptoms after less than a year.

The cases that have been treated since 1929 are also reviewed. A total of 74, or 27 per cent, of the cases sent to the Institute have been treated in this way. Of the 16 cases treated in this way, 12, or 75 per cent, are living and free of symptoms after five to six years; of the 23 treated in 1930, 14, or 60.9 per cent, after four to five years; of the 11 treated in 1931, 5 or 45.4 per cent, after three to four years, and of the 14 treated in 1932, 10, or 71.4 per cent, after two to three years.

There was a marked falling off in the cases treated in 1933 and 1934, probably because the use of the method was limited on account of the considerable number of necroses that occurred. At first too large dosage was used and the method was used in cases in which it was not indicated, for instance in cases in which the cartilage is infiltrated with tumor. The failures are not due to the method as such. For unilateral uncomplicated carcinoma of the vocal cord it is the method of choice.—*Audrey G. Morgan.*

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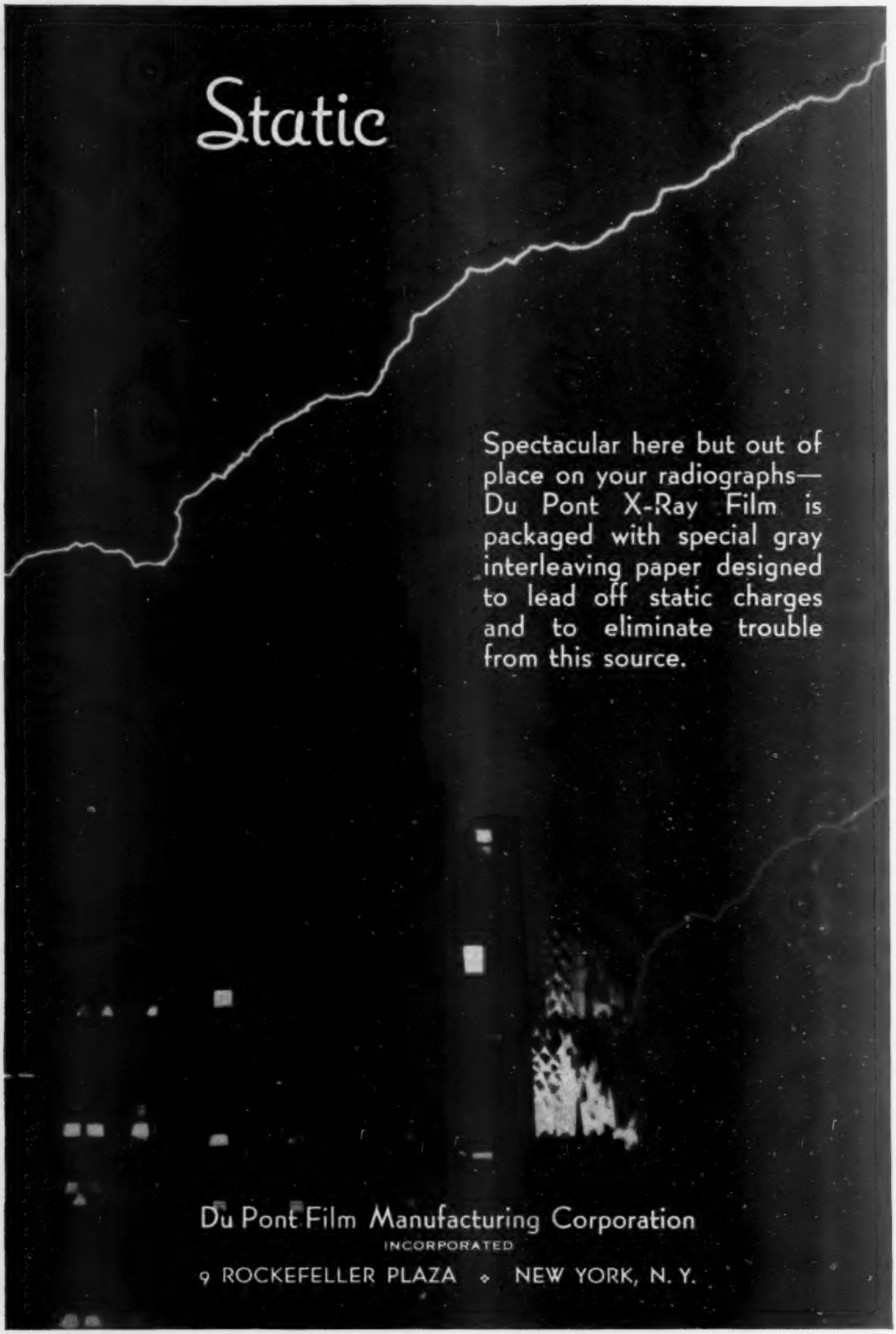
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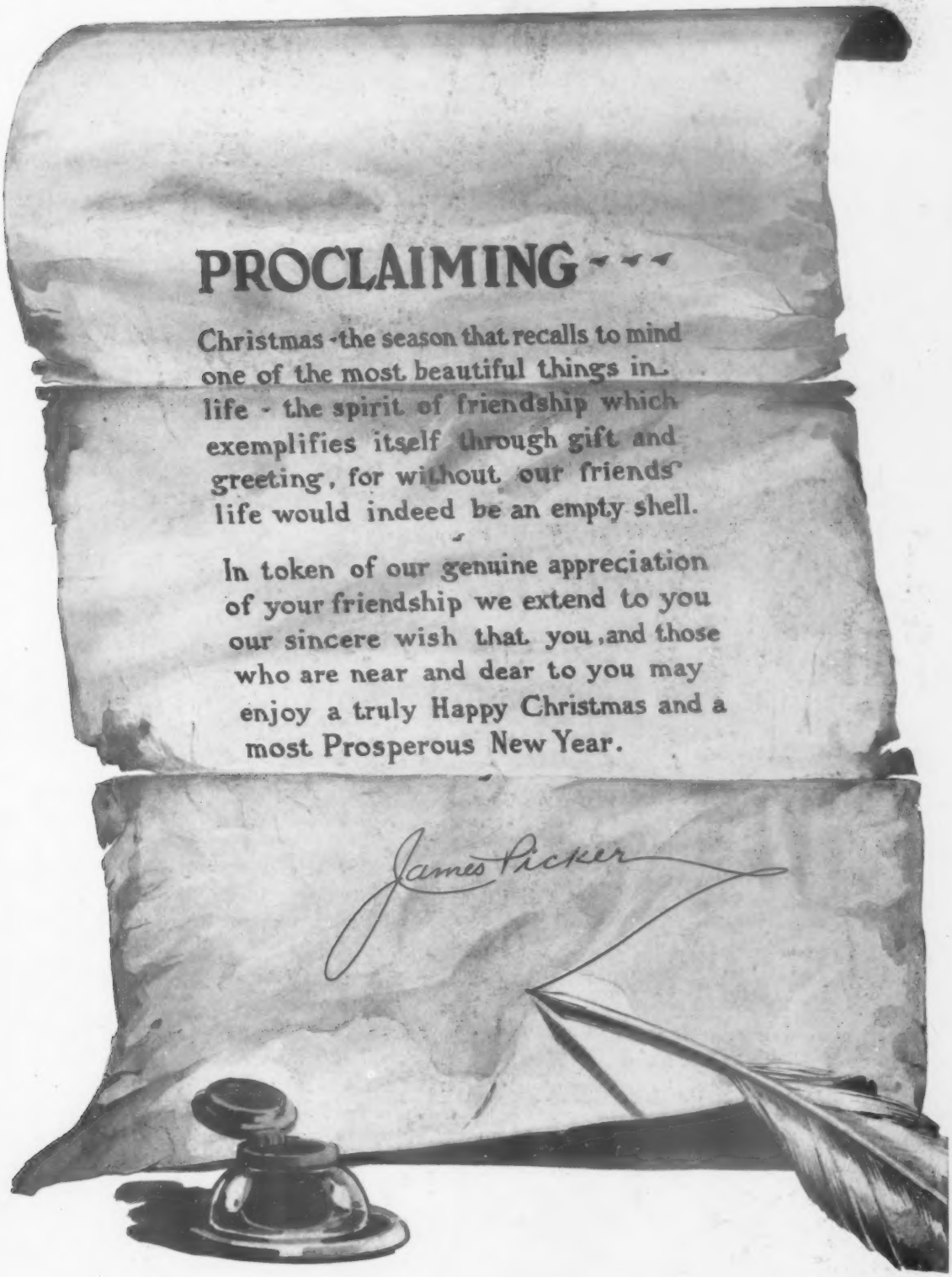
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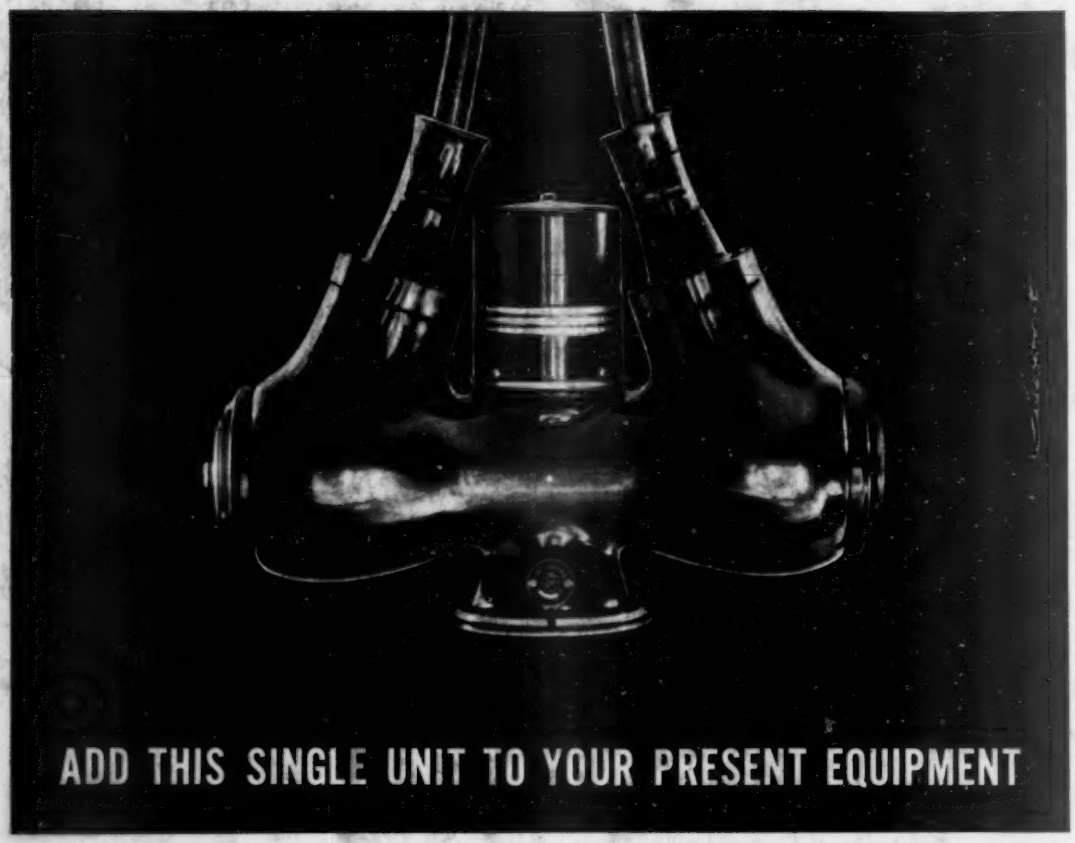

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